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WO 96/41795 (27.12.1996 Gazette 1996/56)

(54) BENZAMIDE DERIVATIVES AND THEIR USE AS VASOPRESSIN ANTAGONISTS

BENZAMID-DERIVATE UND DEREN VERWENDUNG ALS VASOPRESSIN-ANTAGONISTEN

DERIVES DE TYPE BENZAMIDE ET LEUR UTILISATION COMME ANTAGONISTES DE LA VASOPRESSINE

(84) Designated Contracting States:
AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

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(73) Proprietor: **FUJISAWA PHARMACEUTICAL CO., LTD.**
Osaka-shi Osaka 541-8514 (JP)

(72) Inventors:
- **SETOI, Hiroyuki**
  Ibaraki 305 (JP)
- **OHKAWA, Takehiko**
  Ibaraki 300-27 (JP)
- **ZENKOH, Tatsuya**
  Ibaraki 302-01 (JP)
- **SAWADA, Hitoshi**
  Ibaraki 305 (JP)
- **SATO, Kentaro**
  Ibaraki 305 (JP)
- **TANAKA, Hirokazu**
  Hyogo 665 (JP)

(74) Representative:
Gille Hrabal Struck Neidlein Prop Roos
Patentanwälte
Brucknerstrasse 20
40593 Düsseldorf (DE)

(56) References cited:
EP-A- 0 620 216

- **BOLL. CHIM. FARM. (1983), 122(4), 190-5 CODEN: BCFAAI;ISSN: 0006-6648, 1983, XP000601221 PLESCIA, S. ET AL: "A new pyrazolo[4,3-c][1,5]benzodiazocine derivative"**

EP 0 832 061 B1

Description

[0001] This invention relates to new benzamide derivatives and pharmaceutically acceptable salts thereof which are useful as a medicament:.

BACKGROUND ART

[0002] Some benzamide derivatives have been known as vasopressin antagonist, for example, in PCT International Publication Nos. WO 91/05549 and WO 95/29152, and EP Application Publication No. 0620216.

DISCLOSURE OF INVENTION

[0003] This invention relates to new benzamide derivatives and pharmaceutically acceptable salts thereof.

[0004] More particularly, it relates to new benzamide derivatives and pharmaceutically acceptable salts thereof which possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity, oxytocin antagonistic activity and the like, to a pharmaceutical composition comprising the same and the use of the compounds for the manufacture of a medicament for the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, cerebrovascular disease (e.g. cerebral edema, cerebral infarction, etc.), Meniere's syndrome (e.g. Meniere's disease, etc.), motion sickness and the like in human beings or animals.

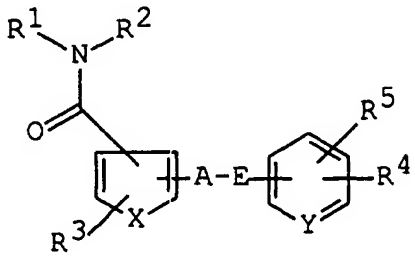
[0005] One object of this invention is to provide new and useful benzamide derivatives which possess aforesaid activities.

[0006] Another object of this invention is to provide processes for the preparation of said benzamide derivatives and salts thereof.

[0007] A further object of this invention is to provide a pharmaceutical composition comprising, as an active ingredient, said benzamide derivatives and pharmaceutically acceptable salts thereof.

[0008] Some benzamide derivatives have been known as vasopressin antagonist, for example, in PCT International Publication Nos. WO 91/05549 and WO 95/29152, and EP Application Publication No. 0620216.

[0009] The object benzamide derivatives of this invention are new and can be represented by the following general formula (I) :



(I)

wherein

R^1 is aryl, cyclo(lower)alkyl, pyridyl or thienyl, each of which may be substituted with substituent(s) selected from the group consisting of halogen; hydroxy; nitro; amino; acyl; substituted acyl; acyl(lower)alkylsulfinyl; acyl(lower)alkylsulfonyl; acyloxy; lower alkylamino(lower)alkylcarbamoyloxy; aryl; cyano; a heterocyclic group;
lower alkenyl optionally substituted with acyl, substituted acyl, aryl or acyl-substituted aryl; lower alkynyl optionally substituted with amino, acylamino or substituted acylamino;
lower alkyl optionally substituted with halogen, amino, lower alkylamino, acylamino, substituted acylamino, hydroxy, acyloxy, acyl(lower)alkanoyloxy, acyl, substituted acyl, acyl(lower)alkoxyimino, aryl or acyl-substituted aryl; lower alkylthio optionally substituted with acyl or substituted acyl;
alkoxy optionally substituted with aryl, substituted aryl, hydroxy, acyloxy, amino, lower alkylamino, protected ami-

no, a heterocyclic group, acyl-substituted pyridyl, substituted acyl-substituted pyridyl, halogen, acyl(lower) alkylamino, N-protected-acyl(lower)alkylamino, N-acyl(lower)alkyl-N-lower alkylamino, acyl, substituted acyl, acylamino, substituted acylamino, lower alkylhydrazinocarbonylamino, hydroxyimino, acyl(lower)alkoxyimino, substituted acyl(lower)alkoxyimino, acyl(lower)alkoxy, guanidino or N-protected guanidino; and
lower alkenyloxy optionally substituted with acyl or substituted acyl;

R^2 is hydrogen; lower alkyl optionally substituted with hydroxy, aryl or acyl; or cyclo(lower)alkyl;

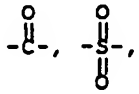
R^3 is hydrogen; halogen; hydroxy; acyloxy; substituted acyloxy; lower alkyl optionally substituted with hydroxy or lower alkoxy; lower alkoxy optionally substituted with aryl, amino, protected amino, acyl, hydroxy, cyano or lower alkylthio; nitro; amino; acyl; substituted acyl; or cyclo(lower)alkyloxy;

R^4 is hydroxy; halogen; nitro; amino; protected amino; lower alkylamino; acyloxy; amino(lower)alkylamino; N-protected amino(lower)alkylamino;
lower alkoxy optionally substituted with hydroxy, aryl, substituted aryl, acyl, substituted acyl, amino, lower alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group or guanidino; lower alkylthio optionally substituted with acyl, substituted acyl, amino, lower alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, lower alkylsulfonyloxy, arylsulfonyloxy, ar(lower)alkoxy or substituted ar(lower)alkoxy; lower alkyl substituted with acyl, substituted acyl, amino, lower alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, lower alkylsulfonyloxy or arylsulfonyloxy; lower alkenyl optionally substituted with acyl; lower alkynyl optionally substituted with hydroxy, amino, protected amino, lower alkylsulfonyloxy or arylsulfonyloxy; amino(lower)alkylsulfonyl; N-protected amino(lower)alkylsulfonyl; lower alkylaminosulfonyl; a heterocyclicsulfonyl; amino(lower)alkylsulfinyl; N-protected amino(lower)alkylsulfinyl; piperidyloxy; or N-protected piperidyloxy;

R^5 is hydrogen, lower alkyl, lower alkoxy or halogen;

A is a single bond, O or NH;

E is lower alkylene, lower alkenylene,



or a group of the formula :

-G-J-

in which G is lower alkylene and J is O or

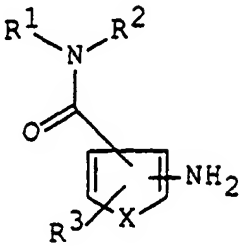
(wherein R^6 is hydrogen or N-protective group) ;

X is -CH=CH-, -CH=N- or S; and
Y is CH or N;

and pharmaceutically acceptable salts thereof.

[0010] The object compound (I) or its salt can be prepared by the processes as illustrated in the following reaction schemes.

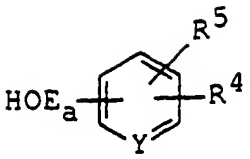
Process 1



(II)

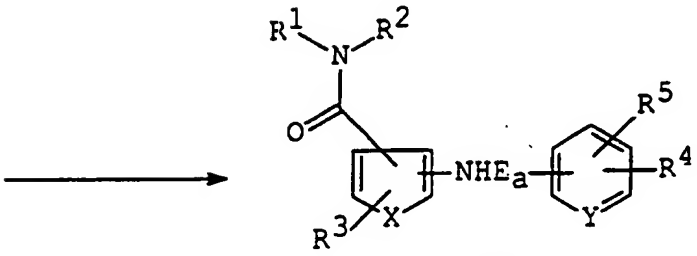
or its salt

+



(III)

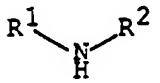
or its reactive derivative at the carboxy group or the sulfo group, or a salt thereof



(Ia)

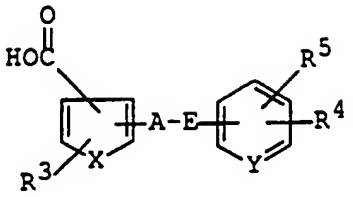
or its salt

Process 2

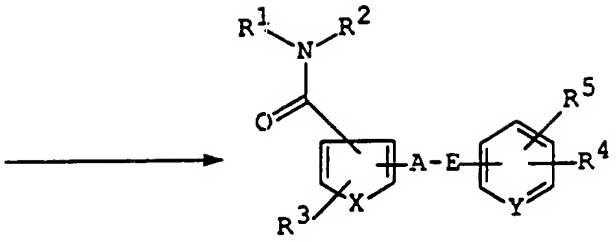


(IV)
or its saslt

+

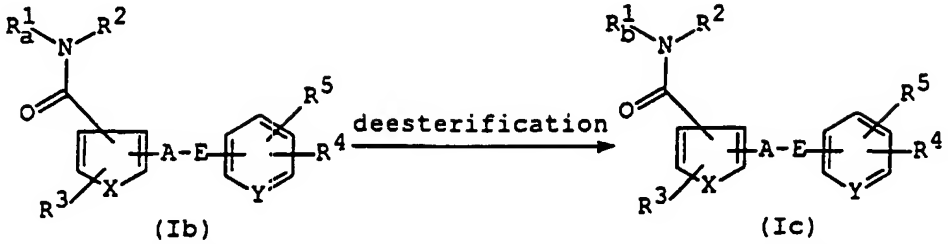


(V)
or its reactive derivative
at the carboxy group
or a salt thereof



(I)
or its salt

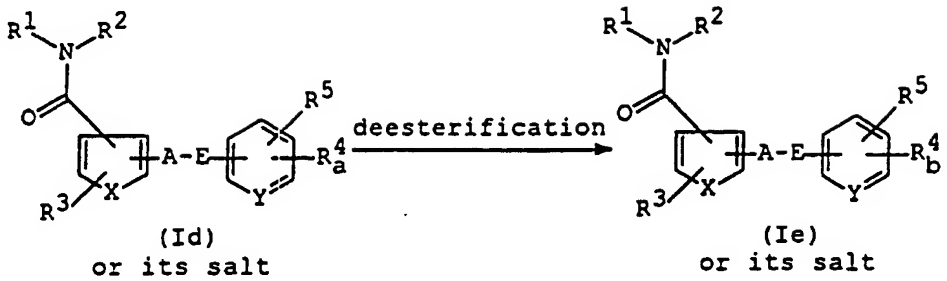
Process 3



(Ib)
or its salt

(Ic)
or its salt

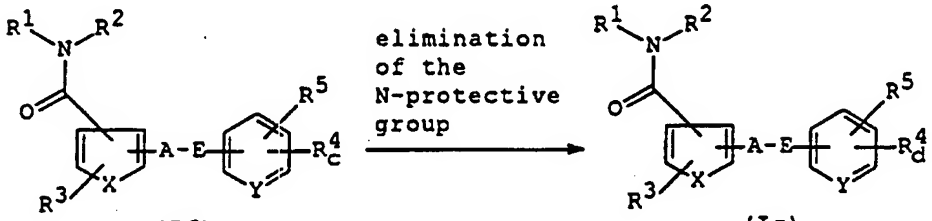
Process 4



(Id)
or its salt

(Ie)
or its salt

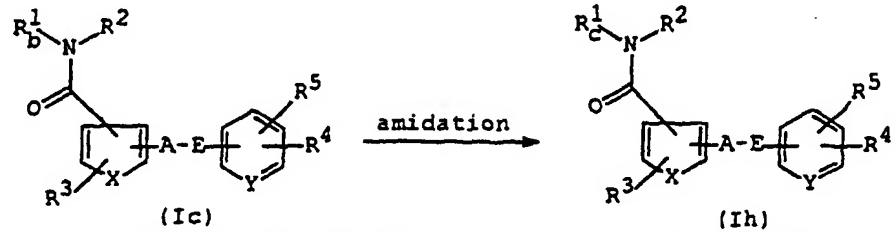
Process 5



(If)
or its salt

(Ig)
or its salt

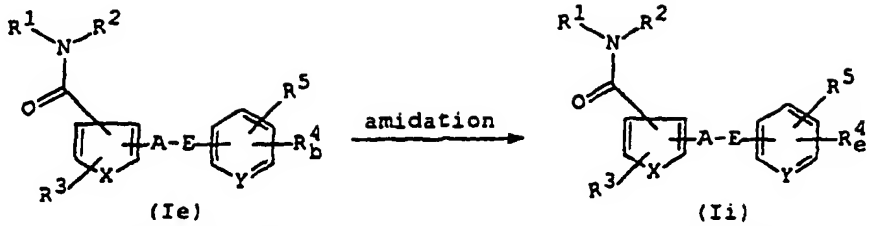
Process 6



(Ic)
or its reactive derivative
at the carboxy group
or a salt thereof

(Ih)
or its salt

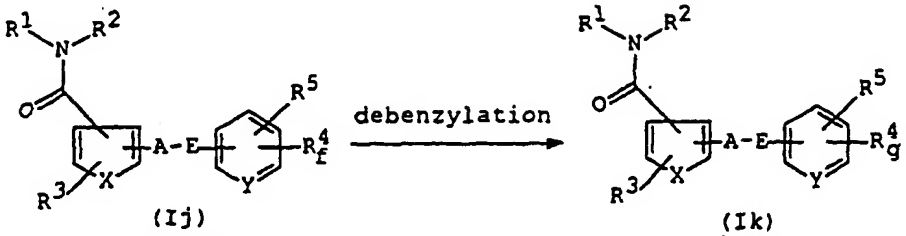
Process 7



(Ie)
or its reactive derivative
at the carboxy group
or a salt thereof

(Ii)
or its salt

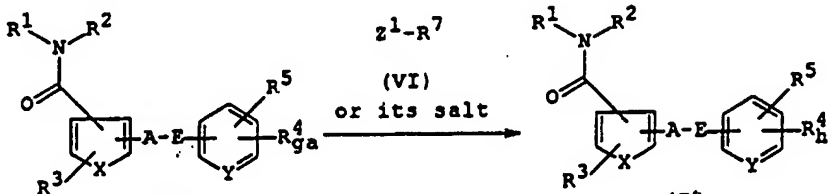
Process 8



(Ij)
or its salt

(Ik)
or its salt

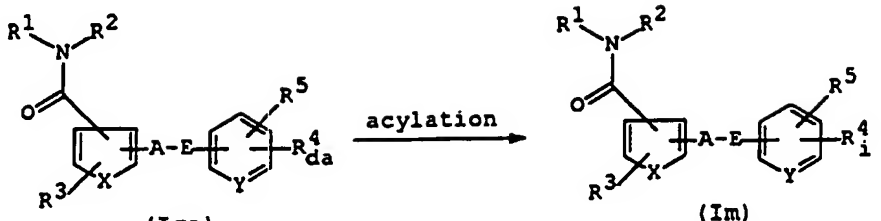
Process 9



(Ika)
or its salt

(I/)
or its salt

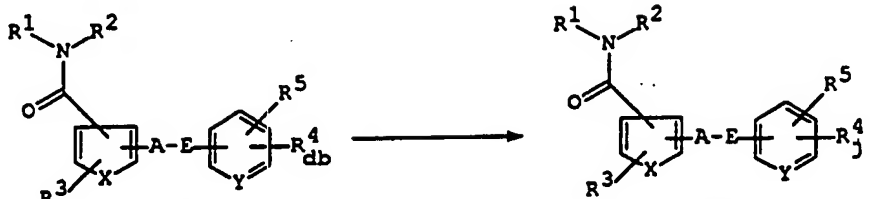
Process 10



(Iga)
or its salt

(Im)
or its salt

Process 11



(Igb)
or its salt

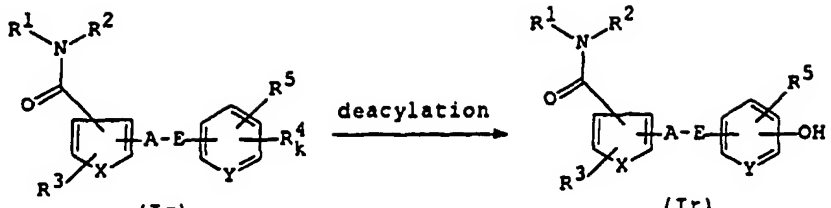
(In)
or its salt

Process 12

(Io)
or its salt

(Ip)
or its salt

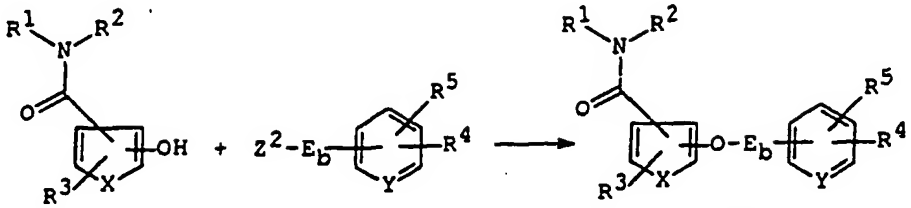
Process 13



(Iq)
or its salt

(Ir)
or its salt

Process 14



(VII)
or its salt

(VIII)
or its salt

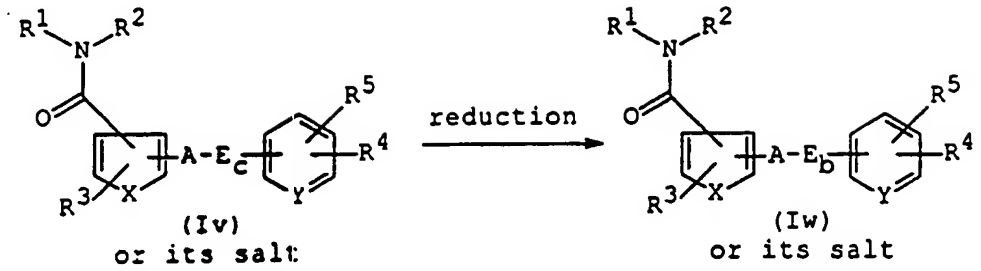
(Is)
or its salt

Process 15

(It)
or its salt

(Iu)
or its salt

Process 16



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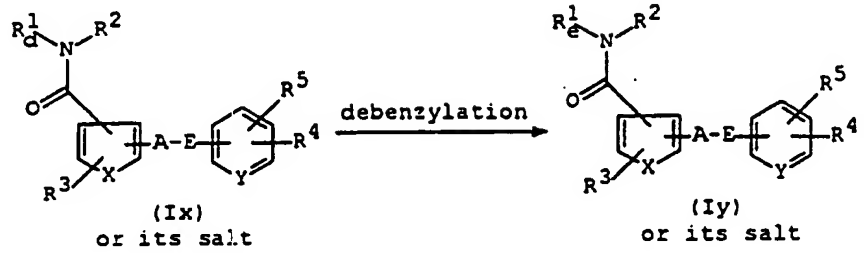

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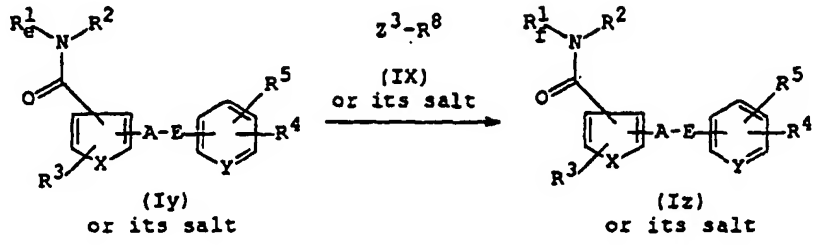
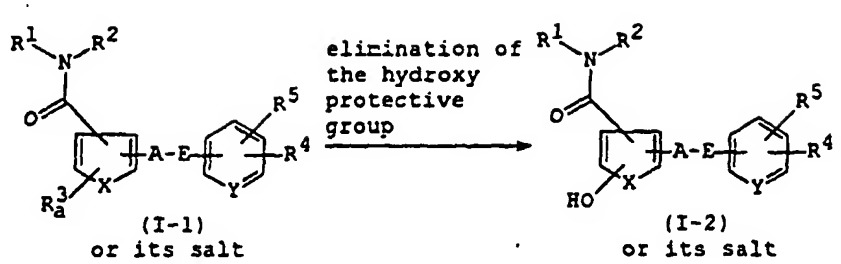


Process 19



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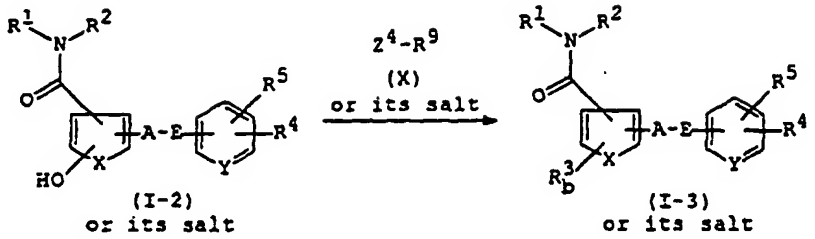

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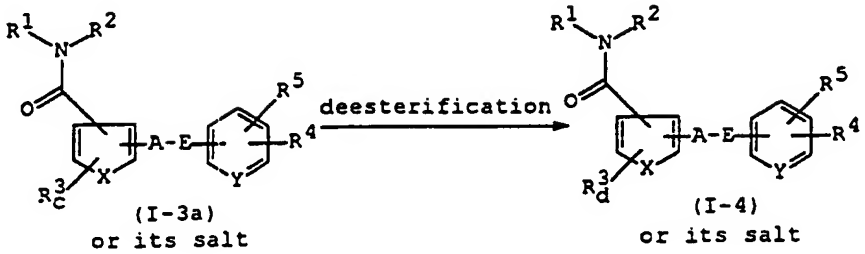

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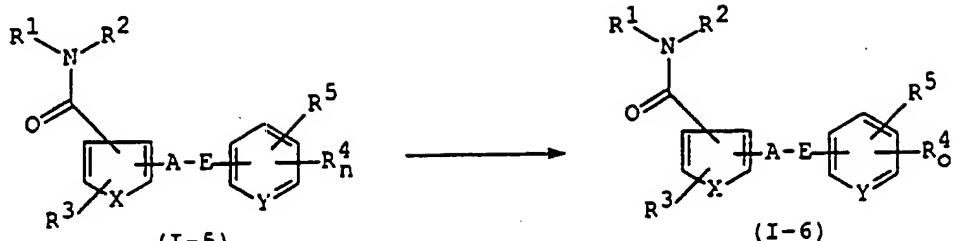
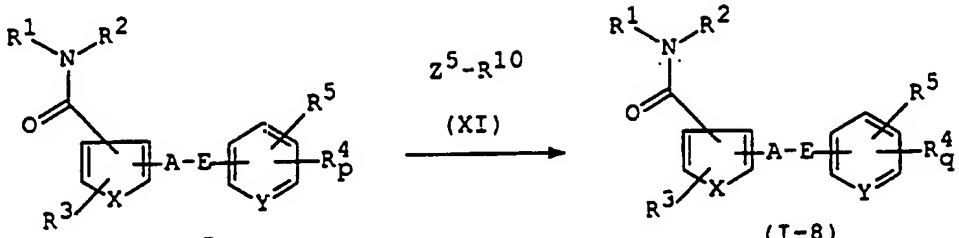


(I-5)
or its salt

(I-6)
or its salt

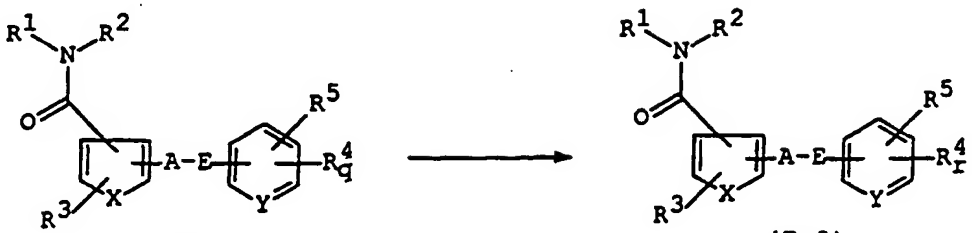
Process 23



(I-7)
or its salt

(I-8)
or its salt

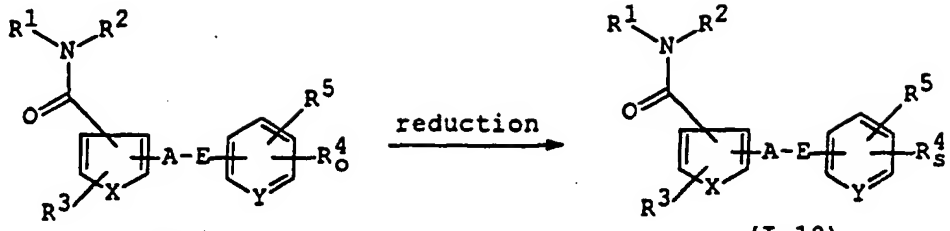
Process 24



(I-8)
or its salt

(I-9)
or its salt

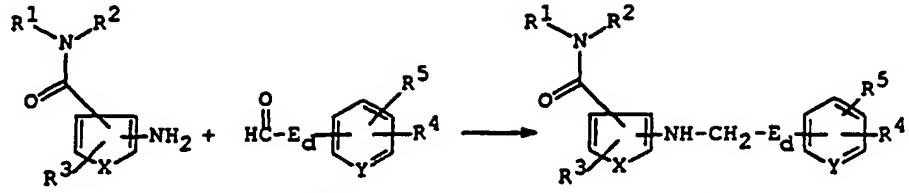
Process 25



(I-6)
or its salt

(I-10)
or its salt

Process 26

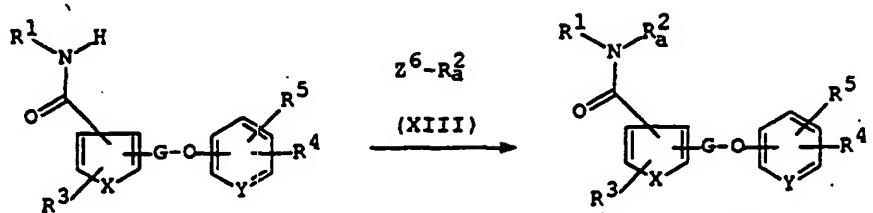


(II)
or its salt

(XII)
or it salt

(I-11)
or its salt

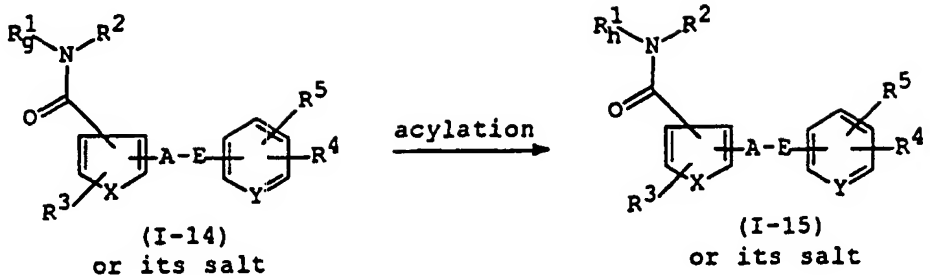
Process 27



(I-12)
or its salt

(I-13)
or its salt

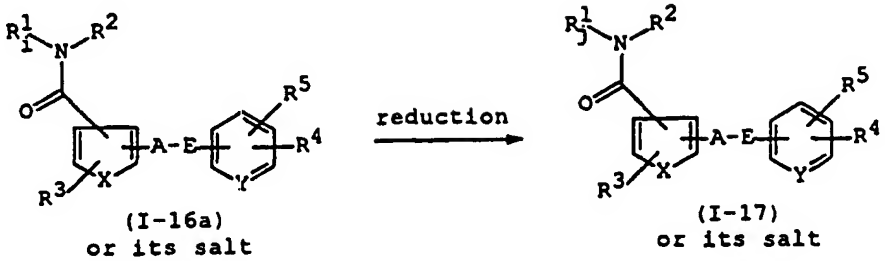
Process 28



(I-14)
or its salt

(I-15)
or its salt

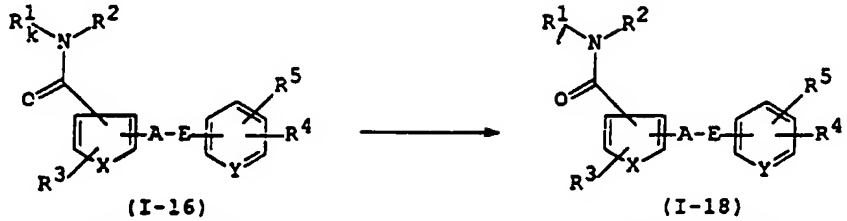
Process 29



(I-16a)
or its salt

(I-17)
or its salt

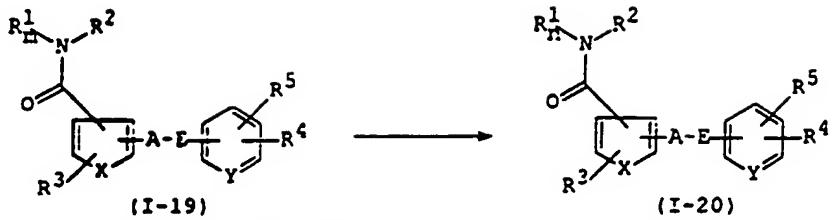
Process 30



(I-16)
or its salt

(I-18)
or its salt

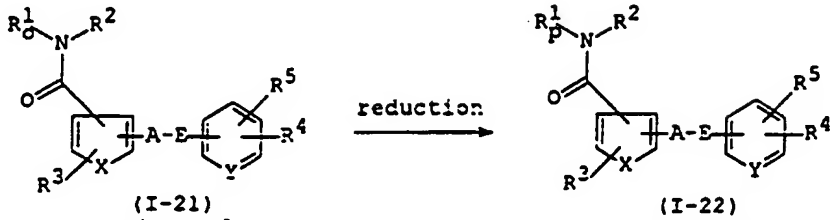
Process 31



(I-19)
or its reactive derivative at the carboxy group or a salt thereof

(I-20)
or its salt

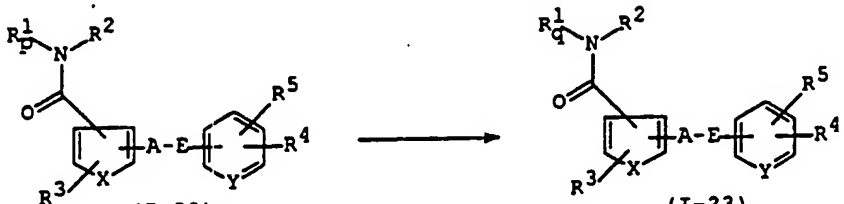
Process 32



(I-21)
or its salt

(I-22)
or its salt

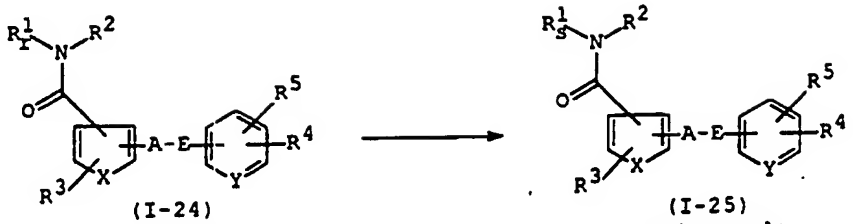
Process 33



(I-22)
or its salt

(I-23)
or its salt

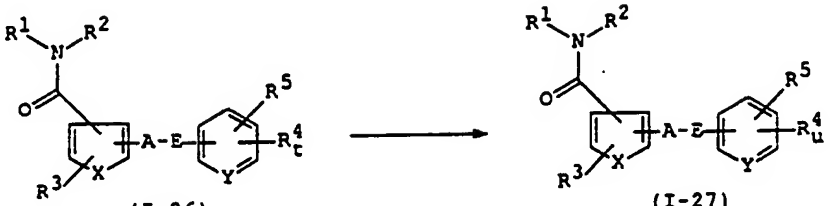
Process 34



(I-24)
or its salt

(I-25)
or its salt

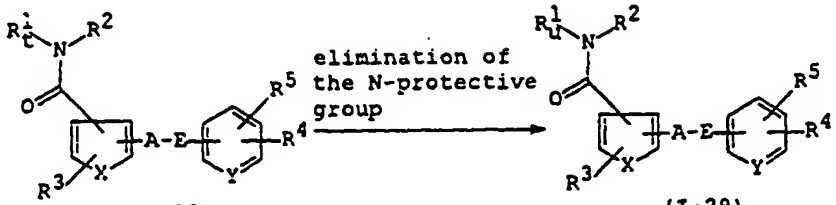
Process 35



(I-26)
or its salt

(I-27)
or its salt

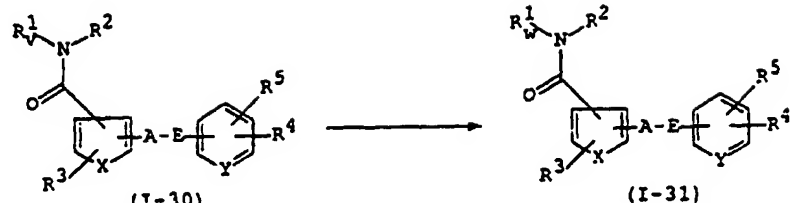
Process 36



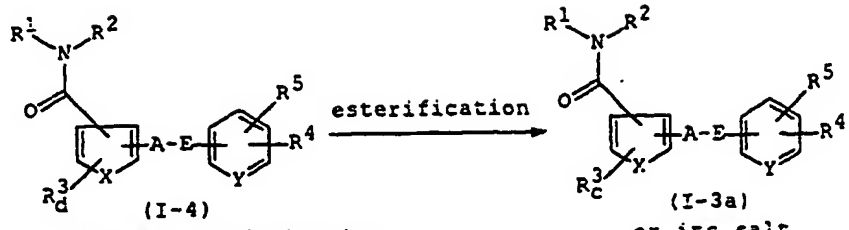
(I-28)
or its salt

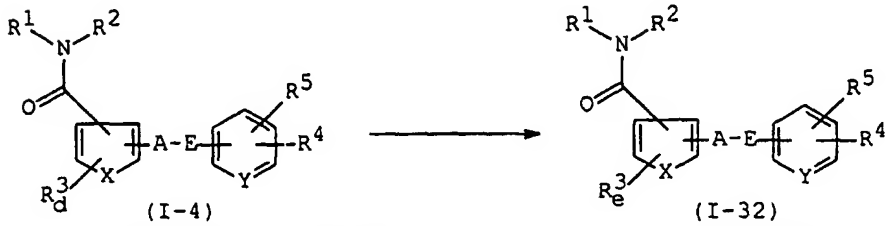
(I-29)
or its salt

Process 37



Process 38

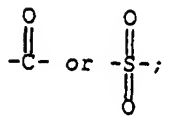




wherein

R^1, R^2, R^3, R^4, R^5, A, E, X and Y are each as defined above,

E_a is



R^1_a is aryl, haloaryl, cyclo(lower)alkyl,
pyridyl or thienyl group, each of which is substituted with esterified carboxy;
lower alkenyl substituted with esterified carboxy or esterified carboxy-substituted aryl;
lower alkyl substituted with esterified carboxy, esterified carboxy(lower)alkanoyloxy or esterified carboxy(lower)alkoxyimino;
lower alkylthio substituted with esterified carboxy; alkoxy substituted with esterified carboxy-substituted aryl, esterified carboxy-substituted pyridyl, esterified carboxy(lower)alkylamino, N-protected-esterified carboxy(lower)alkylamino, N-esterified carboxy(lower)alkyl-N-lower alkylamino, esterified carboxy or esterified carboxy(lower)alkoxyimino; or lower alkenyloxy substituted with esterified carboxy;

R^1_b is aryl, haloaryl, cyclo(lower)alkyl, pyridyl or thienyl, each of which is substituted with carboxy; lower alkenyl substituted with carboxy or carboxy-substituted aryl;
lower alkyl substituted with carboxy, carboxy(lower)-alkanoyloxy or carboxy(lower)alkoxyimino;
lower alkylthio substituted with carboxy;
alkoxy substituted with carboxy-substituted aryl, carboxy-substituted pyridyl, carboxy(lower)-alkylamino, N-protected-carboxy(lower)alkylamino, N-carboxy(lower)alkyl-N-lower alkylamino, carboxy or carboxy(lower)alkoxyimino; or lower alkenyloxy substituted with carboxy;

R^4_a is lower alkoxy substituted with esterified carboxy; lower alkylthio substituted with esterified carboxy; lower alkyl substituted with esterified carboxy; or lower alkenyl substituted with esterified carboxy;

R^4_b is lower alkoxy substituted with carboxy; lower alkylthio substituted with carboxy; lower alkyl substituted with carboxy; or lower alkenyl substituted with carboxy;

R^4_c is protected amino; N-protected piperidyloxy; N-protected amino(lower) alkylamino;
lower alkoxy substituted with protected amino; lower alkylthio substituted with protected amino; lower alkyl substituted with protected amino;
lower alkynyl substituted with protected amino; or N-protected amino(lower)alkylsulfonyl;

R^4_d is amino; piperidyloxy; amino(lower)alkylamino;
lower alkoxy substituted with amino; lower alkylthio substituted with amino; lower alkyl substituted with amino; lower alkynyl substituted with amino;
or amino(lower)alkylsulfonyl;

R^1_c is aryl, haloaryl, cyclo(lower)alkyl, pyridyl or thienyl group, each of which is substituted with substituted
or unsubstituted N-containing heterocycliccarbonyl; carbamoyl; substituted or unsubstituted lower alkylcarbamoyl; lower alkenyl substituted with substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl, substituted or unsubstituted lower alkylcarbamoyl or N-containing heterocycliccarbonyl-substituted aryl;
lower alkyl substituted with substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl, substituted or unsubstituted lower alkylcarbamoyl, substituted or unsubstituted N-containing heterocycliccarbonyl (lower)alkanoyloxy, carbamoyl(lower)alkanoyloxy, substituted or unsubstituted lower alkylcarbamoyl(lower)alkanoyloxy, substituted or unsubstituted N-containing heterocycliccarbonyl (lower)alkoxyimino, carbamoyl-(low-

er)alkoxyimino or substituted or unsubstituted lower alkylcarbamoyl(lower) alkoxyimino;
lower alkylthio substituted with substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl or substituted or unsubstituted lower alkylcarbamoyl; alkoxy substituted with substituted or unsubstituted N-containing heterocycliccarbonyl-substituted aryl, carbamoyl-substituted aryl, substituted or unsubstituted lower alkylcarbamoyl-substituted aryl, substituted or unsubstituted N-containing heterocycliccarbonyl-substituted pyridyl, carbamoyl-substituted pyridyl, substituted or unsubstituted lower alkylcarbamoyl-substituted pyridyl, substituted or unsubstituted N-containing heterocycliccarbonyl (lower)alkylamino, carbamoyl(lower) alkylamino, substituted or unsubstituted lower alkylcarbamoyl(lower) alkylamino, N-protected-(substituted or unsubstituted N-containing heterocyclic)carbonyl(lower)alkylamino, N-protected-carbamoyl(lower) alkylamino, N-protected substituted or unsubstituted lower alkylcarbamoyl (lower)alkylamino, N-(substituted or unsubstituted N-containing heterocyclic)carbonyl(lower)alkyl-N-lower alkylamino, N-carbamoyl(lower)alkyl-N-lower alkylamino, substituted or unsubstituted N-lower alkylcarbamoyl-N-lower alkylamino, substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl, aminocarbamoyl, pyridylcarbamoyl, N-(lower alkyl) piperazinylcarbonyl, substituted or unsubstituted lower alkylcarbamoyl, substituted or unsubstituted N-containing heterocycliccarbonyl(lower) alkoxyimino, carbamoyl(lower)alkoxyimino or substituted or unsubstituted lower alkylcarbamoyl(lower)alkoxyimino;
or lower alkenyloxy substituted with substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl or substituted or unsubstituted lower alkylcarbamoyl;

R^4_e is lower alkoxy, lower alkylthio, lower alkyl or lower alkenyl, each of which is substituted with substituted or unsubstituted N-containing heterocycliccarbonyl, carbamoyl, or substituted or unsubstituted lower alkylcarbamoyl;

R^4_f is methoxy substituted with aryl or substituted aryl; or lower alkylthio which is substituted with methoxy substituted with aryl or substituted aryl;

R^4_g is hydroxy; or lower alkylthio substituted with hydroxy;

R^4_{ga} is hydroxy;

R^7 is lower alkyl substituted with hydroxy, aryl, substituted aryl, acyl, amino, lower alkylamino, acylamino, protected amino or a heterocyclic group; or N-protected piperidyl;

Z^1 is hydroxy; or acid residue;

R^4_h is lower alkoxy substituted with hydroxy, aryl, substituted aryl, acyl, amino, lower alkylamino, acylamino, protected amino or a heterocyclic group; or N-protected piperidyloxy;

R^4_{da} is lower alkoxy substituted with amino; lower alkylthio substituted with amino; or lower alkyl substituted with amino;

R^4_i is lower alkoxy substituted with acylamino or substituted acylamino; lower alkylthio substituted with acylamino or substituted acylamino; or lower alkyl substituted with acylamino or substituted acylamino;

R^4_{db} is amino; lower alkoxy substituted with amino; lower alkylthio substituted with amino; or lower alkyl substituted with amino;

R^4_j is lower alkoxy substituted with lower alkylamino; lower alkylthio substituted with lower alkylamino; lower alkyl substituted with lower alkylamino; lower alkylamino; or N-protected amino(lower)alkylamino;

R^4_k is acyloxy;

Z^2 is acid residue;

E_b is lower alkylene;

R^4_ℓ is lower alkylthio substituted with amino or protected amino;

R^4_m is lower alkylsulfinyl substituted with amino or protected amino, or lower alkylsulfonyl substituted with amino or protected amino;

E_c is lower alkenylene;

R^1_d is aryl which is substituted with methoxy substituted with aryl or substituted aryl;

R^1_e is aryl which is substituted with hydroxy;

Z^3 is hydroxy; or acid residue;

R^8 is lower alkyl optionally substituted with acyl, acylamino, protected amino, aryl, substituted aryl, acyl-substituted pyridyl or N-protected guanidino;

R^1_f is aryl which is substituted with lower alkoxy optionally substituted with acyl, acylamino, protected amino, aryl, substituted aryl, acyl-substituted pyridyl or N-protected guanidino;

R^3_a is methoxy substituted with aryl; acyloxy; or substituted acyloxy;

Z^4 is acid residue;

R^9 is lower alkyl optionally substituted with esterified carboxy;

R^3_b is lower alkoxy optionally substituted with esterified carboxy;

R^3_c is lower alkoxy substituted with esterified carboxy;

R^3_d is lower alkoxy substituted with carboxy;

R^4_n is halogen;

R^4_o is lower alkynyl optionally substituted with hydroxy, amino, protected amino, lower alkylsulfonyloxy or arylsulfonyloxy;

R^4_p is lower alkylthio, lower alkyl or lower alkynyl, each of which is substituted with hydroxy;

Z^5 is halogen;

R^{10} is lower alkylsulfonyl or arylsulfonyl;

R^4_q is lower alkylthio, lower alkyl or lower alkynyl, each of which is substituted with lower alkylsulfonyloxy or arylsulfonyloxy;

R^4_r is lower alkylthio, lower alkyl or lower alkynyl, each of which is substituted with phthalimido;

R^4_s is lower alkyl optionally substituted with hydroxy, amino, protected amino, lower alkylsulfonyloxy or arylsulfonyloxy;

E_d is a single bond or lower alkylene;

Z^6 is acid residue;

R^2_a is lower alkyl optionally substituted with aryl or acyl;

R^1_g is aryl which is substituted with lower alkoxy substituted with amino;

R^1_h is aryl which is substituted with lower alkoxy substituted with acylamino or substituted acylamino;

R^1_i is aryl which is substituted with lower alkoxy substituted with oxopiperidylcarbonyl;

R^1_j is aryl which is substituted with lower alkoxy substituted with hydroxypiperidylcarbonyl;

R^1_k is aryl which is substituted with lower alkoxy substituted with formyl or oxopiperidylcarbonyl;

R^1_ℓ is aryl which is substituted with lower alkoxy substituted with aminopiperidylcarbonyl or N-lower alkylpiperazinyl;

R^1_m is aryl which is substituted with lower alkoxy substituted with carboxy;

R^1_n is aryl which is substituted with lower alkoxy substituted with lower alkylamino(lower)-alkoxycarbonyl;

R^1_o is aryl which is substituted with lower alkoxy substituted with esterified carboxy;

R^1_p is aryl which is substituted with lower alkoxy substituted with hydroxy;

R^1_q is aryl which is substituted with lower alkoxy substituted with formyl;

R^1_r is aryl which is substituted with lower alkoxy substituted with cyano-substituted aryl;

R^1_s is aryl which is substituted with lower alkoxy substituted with tetrazolyl-substituted aryl;

R^4_t is lower alkoxy substituted with amino;

R^4_u is lower alkoxy substituted with guanidino;

R^1_t is aryl which is substituted with lower alkoxy substituted with protected amino, N-protected amino (lower) alkanoylamino, N-protected piperazinylcarbonyl or N-protected guanidino;

R^1_u	is aryl which is substituted with lower alkoxy substituted with amino, amino (lower)alkanoylamino, piperazinylcarbonyl or guanidino;
R^1_v	is aryl which is substituted with lower alkoxy substituted with phenoxycarbonylamino;
R^1_w	is aryl which is substituted with lower alkoxy substituted with N-lower alkylpiperazinylcarbonylamino, dimethylaminopiperidylcarbonylamino, carbamoylamino or dimethylcarbamoylamino; and
R^3_e	is lower alkoxy which is substituted with carbamoyl optionally substituted with lower alkyl.

[0011] In the above and subsequent description of the present specification, suitable examples of the various definitions to be included within the scope of the invention are explained in detail in the following.

[0012] The term "lower" is intended to mean a group having 1 to 6 carbon atom(s), unless otherwise provided.

[0013] The "higher" is intended to mean 7 to 20 carbon atoms, unless otherwise provided.

[0014] The lower moiety in the terms "cyclo(lower)alkyl" and "cyclo(lower)alkyloxy" is intended to mean a group having 3 to 6 carbon atoms.

[0015] The lower moiety in the terms "lower alkenyl", "lower alkenyloxy" and "lower alkynyl" is intended to mean a group having 2 to 6 carbon atoms.

[0016] The term "alkoxy" may included lower alkoxy and higher alkoxy.

[0017] Suitable "lower alkoxy" and lower alkoxy moiety in the terms "acyl(lower)alkoxy", "acyl(lower)alkoxyimino", "esterified carboxy(lower)alkoxyimino", "carboxy(lower)alkoxyimino", "N-containing heterocycliccarbonyl(lower)alkoxyimino", "carbamoyl (lower)alkoxyimino", "lower alkylcarbamoyl-(lower)alkoxyimino", "lower alkoxycarbonyl" and "ar(lower)alkoxy" may be straight or branched C_1-C_6 alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, methylpropoxy, butoxy, isobutoxy, tert-butoxy, pentyloxy, hexyloxy or the like.

[0018] Suitable "higher alkoxy" may be straight or branched C_7-C_{20} alkoxy such as heptyloxy, octyloxy, nonyloxy, decyloxy, undecyloxy, dodecyloxy, tridecyloxy, tetradecyloxy, pentadecyloxy, hexadecyloxy, heptadecyloxy, octadecyloxy, nonadecyloxy, eicosyloxy, methylheptyloxy, methyloctyloxy, methylnonyloxy, methyldecyloxy, ethylheptyloxy, ethyloctyloxy, ethylnonyloxy, ethyldecyloxy or the like, in which preferable one is heptyloxy.

[0019] Suitable "lower alkyl" and lower alkyl moiety in the terms "acyl(lower)alkylsulfinyl", "acyl(lower)alkylsulfonyl", "lower alkylamino(lower)alkylcarbamoyloxy", "acyl(lower)alkylamino", "N-protected-acyl(lower)-alkylamino", "N-acyl(lower)alkyl-N-lower alkylamino", "lower alkylhydrazinocarbonylamino", "esterified carboxy(lower)alkylamino", "N-protected-esterified carboxy(lower)alkylamino", "N-esterified carboxy(lower)alkyl-N-lower alkylamino", "carboxy(lower)alkylamino", "N-protected-carboxy(lower)-alkylamino", "N-carboxy(lower)alkyl-N-lower alkylamino", "lower alkylcarbamoyl", "lower alkylcarbamoyl(lower)alkanoyloxy", "lower alkylcarbamoyl(lower)alkoxyimino", "lower alkylthio", "N-protected-(substituted or unsubstituted N-containing heterocyclic)carbonyl (lower)alkylamino", "N-protected-carbamoyl(lower)alkylamino", "N-protected-substituted or unsubstituted lower alkylcarbamoyl(lower)alkylamino", "N-(substituted or unsubstituted N-containing heterocyclic)carbonyl(lower)alkyl-N-lower alkylamino", "N-carbamoyl(lower)alkyl-N-lower alkylamino", "N-lower alkylcarbamoyl-N-lower alkylamino", "lower alkylcarbamoyl-(lower)alkoxyimino", "1-hydroxy(lower)alkyl", "1-(lower alkyl)amino(lower) alkyl", "mono(lower)alkylamino", "acyl(lower)alkyl", "di(lower)alkylamino", "lower alkylsulfinyl", "lower alkylsulfonyl", "lower alkylamino", "amino(lower)alkylamino", "N-protected amino(lower)alkylamino", "lower alkylsulfonyloxy", "amino(lower)alkylsulfonyl", "N-protected amino(lower)alkylsulfonyl", "lower alkylaminosulfonyl", "amino(lower)alkylsulfinyl" and "N-protected amino(lower)alkylsulfinyl" may be straight or branched C_1-C_6 alkyl such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, ethylpropyl, hexyl or the like.

[0020] Suitable "cyclo(lower)alkyl" and cyclo(lower)alkyl moiety in the term "cyclo(lower)alkyloxy" may be cyclo(C_3-C_6)alkyl such as cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, in which preferable one is cyclopentyl or cyclohexyl.

[0021] Suitable "lower alkenyl" and lower alkenyl moiety in the term "lower alkenyloxy" may be straight and branched C_2-C_6 alkenyl such as ethenyl, propenyl, pentenyl, isopropenyl, butenyl, hexenyl or the like, in which preferable one is ethenyl, propenyl, pentenyl or hexenyl.

[0022] Suitable "lower alkynyl" may be straight and branched C_2-C_6 alkynyl such as ethynyl, propargyl, butynyl or the like, in which preferable one is butynyl.

[0023] Suitable "aryl" and aryl moiety in the terms "haloaryl", "arylsulfonyl", "acyl-substituted aryl", "ar(lower)alkoxy", "substituted ar(lower)alkoxy" and "arylsulfonyloxy" may be phenyl, naphthyl, phenyl substituted with lower alkyl [e.g. tolyl, xylyl, mesityl, cumenyl, di(tert-butyl)phenyl, etc.] and the like, in which preferable one is phenyl, tolyl or xylyl.

[0024] Suitable "substituted aryl" may be aryl substituted with suitable substituent(s) such as acyl, substituted acyl, N-protected piperazinylsulfonyl, piperazinylsulfonyl, N-lower alkylpiperazinylsulfonyl, hydroxy(lower)alkyl, a heterocyclic(lower)alkyl, halogen, nitro, amino, lower alkylamino, a heterocyclic group [e.g. thiazolyl, oxazolyl, tetrazolyl, oxazolinyl, pyridyl, pyrimidinyl, pyrrolyl optionally substituted with lower alkyl and cyano, etc.], cyano, lower alkoxy or the

like, in which preferable one for the substituent of alkoxy for R^1 is aryl substituted with N-methylpiperazinylsulfonyl, N-t-butoxycarbonylpiperazinylsulfonyl, piperazinylsulfonyl, carboxy, esterified carboxy, N-lower alkylpiperazinylcarbonyl, lower alkanoyl, hydroxy(lower)alkyl, N-lower alkylpiperazinyl(lower)alkyl, thiazolyl, oxazolyl, tetrazolyl, oxazolinyl, pyridyl, pyrimidinyl, pyrrolyl substituted with lower alkyl and cyano, cyano, lower alkoxy, lower alkylaminopiperidylcarbonyl, and preferable one for R^4 is aryl substituted with halogen, nitro, amino, lower alkylamino or lower alkoxy.

[0025] Suitable "halogen" and halo moiety in the term "haloaryl" may be fluorine, chlorine, bromine and iodine, in which preferable one is chlorine or bromine.

[0026] Suitable "lower alkylamino" and lower alkylamino moiety in the terms "lower alkylamino(lower)-alkylcarbamoyloxy", "acyl(lower)alkylamino", "esterified carboxy(lower)alkylamino", "carboxy(lower)alkylamino", "N-containing heterocycliccarbonyl(lower)alkylamino", "carbamoyl(lower)alkylamino", "lower alkylcarbamoyl(lower)alkylamino" "amino (lower)alkylamino", "N-protected amino(lower)alkylamino", "lower alkylaminosulfonyl" and "lower alkylaminopiperidylcarbonyl" may be mono or di(lower alkyl)amino such as methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, isobutylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, diisopropylamino, dipentylamino, dihexylamino, N-methylethylamino or the like, in which preferable one is methylamino, dimethylamino or diethylamino.

[0027] Suitable "1-hydroxy(lower)alkyl" may be 1-hydroxy-(C_1-C_6)alkyl such as hydroxymethyl, 1-hydroxyethyl, 1-hydroxypropyl, 1-hydroxybutyl, 1-hydroxy-3-methylpropyl or the like, in which preferable one is hydroxymethyl or 1-hydroxyethyl.

[0028] Suitable "1-(lower alkyl)amino(lower)alkyl" may be 1-mono or di(C_1-C_6 alkyl)amino(C_1-C_6)alkyl such as methylaminomethyl, dimethylaminomethyl, 1-methylaminoethyl, 1-dimethylaminoethyl, ethylaminomethyl, 1-ethylaminoethyl or the like, in which preferable one is methylaminomethyl, dimethylaminomethyl, 1-methylaminoethyl or 1-dimethylaminoethyl.

[0029] Suitable "heterocyclic group" may be one containing at least one hetero atom selected from nitrogen, sulfur and oxygen atom, and may include saturated or unsaturated, monocyclic or polycyclic heterocyclic group, and preferable heterocyclic group may be N-containing heterocyclic group such as unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl [e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.], tetrazolyl [e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.], etc.;

saturated 3 to 7-membered heteromonocyclic group containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, homopiperazinyl, etc.]; unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, imidazopyridyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g. tetrazolo[1,5-b]pyridazinyl, etc.], etc.; unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, furyl, etc.;

saturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, 1H-tetrahydropyranyl, tetrahydrofuranyl, etc.; unsaturated, 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms, for example, thienyl, etc.; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.], oxazolinyl [e.g. 2-oxazolinyl, etc.], etc.; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl, etc.];

unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzofurazanyl, benzoxazolyl, benzoxadiazolyl, etc.]; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.], etc.;

saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl, etc.];

unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.];

unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms [e.g. benzofuranyl, benzodioxolyl, etc.] and the like.

[0030] Said "heterocyclic group" may be substituted with lower alkyl as exemplified above or oxo, in which preferable one is N-methylpiperazinyl, tetrazolyl, morpholinyl, pyrrolidinyl, N-methylpiperidyl, N-methylhomopiperazinyl, 1H-tetrahydropyranyl, thienyl, pyridyl, piperidyl or oxopiperidyl.

[0031] Suitable acyl and acyl moiety in the terms "acyl (lower)alkylsulfinyl", "acyl(lower)alkylsulfonyl", "acyloxy", "acylamino", "acyl(lower)alkanoyloxy", "acyl(lower)alkoxyimino", "acyl(lower)alkylamino", "N-protected-acyl(lower) alkylamino", "N-acyl(lower)alkyl-N-lower alkylamino" and "acyl(lower)alkoxy" may be carboxy, esterified carboxy, carbamoyl, lower alkylcarbamoyl, lower alkanoyl, aroyl, a heterocycliccarbonyl and the like.

[0032] The esterified carboxy may be substituted or unsubstituted lower alkoxycarbonyl [e.g. methoxycarbonyl,

ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, hexyloxycarbonyl, 2-iodoethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, dimethylaminopropoxycarbonyl, dimethylaminoethoxycarbonyl, etc.], substituted or unsubstituted aryloxycarbonyl [e.g. phenoxycarbonyl, 4-nitrophenoxycarbonyl, 2-naphthyloxycarbonyl, etc.], substituted or unsubstituted ar(lower)alkoxycarbonyl [e.g. benzyloxycarbonyl, phenethyloxycarbonyl, benzhydryloxycarbonyl, 4-nitrobenzyloxycarbonyl, 3-methoxy-4-nitrobenzyloxycarbonyl, etc.], N-containing heterocyclicoxycarbonyl [e.g. N-methylpiperidyloxycarbonyl, etc.] and the like, in which preferable one is lower alkoxycarbonyl, N-methylpiperidyloxycarbonyl, dimethylaminopropoxycarbonyl or dimethylaminoethoxycarbonyl.

[0033] The lower alkylcarbamoyl may be mono or di(lower alkyl)carbamoyl such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, dimethylcarbamoyl, diethylcarbamoyl, N-methyl-N-ethylcarbamoyl or the like.

[0034] The lower alkanoyl may be substituted or unsubstituted C_1-C_6 alkanoyl such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, trifluoroacetyl or the like, in which preferable one is formyl, acetyl or butyryl.

[0035] The aroyl may be benzoyl, naphthoyl, toluoyl, di(tert-butyl)benzoyl and the like, in which preferable one is benzoyl.

[0036] The heterocyclic moiety in the terms "a heterocycliccarbonyl", "heterocyclicoxycarbonylamino" and "heterocyclicsulfonyl" may be one mentioned above as a heterocyclic group.

[0037] Preferred "a heterocycliccarbonyl" may be N-containing heterocycliccarbonyl.

[0038] The "N-containing heterocycliccarbonyl" may be one containing at least one nitrogen atom in heterocyclic group mentioned above, in which preferable one is N-(lower alkyl)piperazinylcarbonyl (e.g. N-methylpiperazinylcarbonyl, etc.), N-(lower alkyl)-homopiperazinylcarbonyl (e.g. N-methylhomopiperazinylcarbonyl, etc.), piperazinylcarbonyl, pyrrodinylcarbonyl, piperidylcarbonyl, morpholinocarbonyl, lower alkylpiperidylcarbonyl (e.g. methylpiperidylcarbonyl, etc.) or oxopiperidylcarbonyl.

[0039] Suitable "substituted acyl" may be carbamoyl substituted with amino, a heterocyclic group [e.g. N-(lower alkyl) piperazinyl, pyridyl, etc.], lower alkylsulfonyl or arylsulfonyl, substituted lower alkylcarbamoyl [e.g. N-lower alkylamino-N-lower alkylcarbamoyl, pyridyl(lower)alkylcarbamoyl, morpholino(lower)alkylcarbamoyl, bis[hydroxy(lower)alkyl]carbamoyl, hydroxy(lower)alkylcarbamoyl, carbamoyl(lower)alkylcarbamoyl, lower alkylamino(lower)alkylcarbamoyl, N-lower alkyl-N-lower alkylcarbamoyl, etc.], substituted N-containing heterocycliccarbonyl [e.g. trifluoroacetylpiperazinylcarbonyl, pyridylpiperazinylcarbonyl, hydroxypiperidylcarbonyl, dimethylaminopiperidylcarbonyl, diethylaminopiperidylcarbonyl, carbamoylpyrrolidinylcarbonyl, dimethylaminopiperazinylcarbonyl, hydroxyethoxyethylpiperazinylcarbonyl, pyrrolidinylcarbonylmethylpiperazinylcarbonyl, etc.], N-protected-N-containing heterocycliccarbonyl [e.g. N-t-butoxycarbonylpiperidylcarbonyl, N-t-butoxycarbonylpiperazinylcarbonyl, etc.], N-protected amino(lower)alkanoyl, amino (lower)alkanoyl, benzyloxybenzoyl, and the like.

[0040] "N-Protective group" in "protected amino" may be common N-protective group such as substituted or unsubstituted lower alkanoyl [e.g. formyl, acetyl, propionyl, trifluoroacetyl, etc.], phthaloyl, lower alkoxycarbonyl [e.g. tert-butoxycarbonyl, tert-amyloxycarbonyl, etc.], substituted or unsubstituted aralkyloxycarbonyl [e.g. benzyloxycarbonyl, p-nitrobenzyloxycarbonyl, etc.], 9-fluorenylmethoxycarbonyl, substituted or unsubstituted arenesulfonyl [e.g. benzenesulfonyl, tosyl, etc.], nitrophenylsulfenyl, aralkyl [e.g. trityl, benzyl, etc.] or the like, in which preferable one is phthaloyl, tert-butoxycarbonyl or 9-fluorenylmethoxycarbonyl.

[0041] "N-protective group" in "N-protected guanidino" may be common N-protective group such as lower alkoxycarbonyl [e.g. tert-butoxycarbonyl, etc.] or the like.

[0042] Suitable "acid residue" may be halogen [e.g. fluoro, chloro, bromo, iodo], arenesulfonyloxy [e.g. benzenesulfonyloxy, tosyloxy, etc.], alkanesulfonyloxy [e.g. mesyloxy, ethanesulfonyloxy, etc.], and the like, in which preferable one is halogen.

[0043] Suitable "lower alkylsulfonyl" and lower alkylsulfonyl moiety in the term "lower alkylsulfonyloxy" may be (C_1-C_6)alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, propylsulfonyl or the like, in which preferable one is methylsulfonyl.

[0044] Suitable "lower alkylene" may be straight or branched C_1-C_6 alkylene such as methylene, ethylene, propylene or the like, in which preferable one is methylene or ethylene.

[0045] Suitable "lower alkenylene" may be straight or branched C_2-C_6 alkenylene such as ethenylene, propenylene or the like, in which preferable one is ethenylene.

[0046] The substituent(s) on aryl for R^1 may be plural and in such case the substituents may be the same or different.

[0047] Preferred "aryl" for R^1 may be phenyl or phenyl substituted with lower alkyl.

[0048] Preferred "cyclo(lower)alkyl" for R^1 may be cyclopentyl.

[0049] Preferred compound (I) is one having aryl (more preferably phenyl or phenyl substituted with lower alkyl) which may be substituted with lower alkoxy optionally substituted with acylamino or acyl for R^1, lower alkyl for R^2, hydrogen, lower alkyl or lower alkoxy for R^3, hydroxy, or lower alkoxy, lower alkylthio or lower alkyl, each of which may be substituted with hydroxy, aryl, substituted aryl, acyl, amino, lower alkylamino, acylamino, protected amino or a heterocyclic group for R^4, hydrogen, lower alkyl, lower alkoxy or halogen for R^5, NH for A,

for E, -CH=CH- for X, and CH for Y.

[0050] More preferred compound (I) is one having phenyl or tolyl, each of which is substituted with lower alkoxy substituted with N-(lower alkyl)piperazinylcarbonyl for R^1, lower alkyl for R^2, hydrogen, lower alkyl or lower alkoxy for R^3, lower alkoxy substituted with amino for R^4, hydrogen for R^5, NH for A,

for E, -CH=CH- for X and CH for Y.

[0051] Most preferred compound (I) is one having tolyl which is substituted with lower alkoxy substituted with N-(lower alkyl)piperazinylcarbonyl for R^1, lower alkyl for R^2, lower alkoxy for R^3, lower alkoxy substituted with amino for R^4, hydrogen for R^5, NH for A,

for E, -CH=CH- for X and CH for Y.

[0052] Suitable pharmaceutically acceptable salts of the object compound (I) are conventional non-toxic salts and include an acid addition salt such as an inorganic acid addition salt [e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.], an organic acid addition salt [e.g. formate, acetate, trifluoroacetate, maleate, tartrate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.], a metal salt such as an alkali metal salt [e.g. sodium salt, potassium salt, etc.] and an alkaline earth metal salt [e.g. calcium salt, magnesium salt, etc.] and the like.

[0053] The processes for preparing the object compound (I) are explained in detail in the following.

Process 1

[0054] The object compound (Ia) or its salt can be prepared by reacting a compound (II) or its salt with a compound (III) or its reactive derivative at the carboxy group or the sulfo group, or a salt thereof.

[0055] Suitable salts of the compounds (Ia) and (II) may be the same as those exemplified for the compound (I).

[0056] Suitable salts of the compound (III) and its reactive derivative at the carboxy group or the sulfo group may be base salts as exemplified for the compound (I).

[0057] Suitable reactive derivative at the carboxy group or the sulfo group of the compound (III) may include an acid halide, an acid anhydride containing intramolecular, intermolecular and a mixed ones, an activated amide, an activated ester, and the like. Suitable examples of the reactive derivatives may be an acid chloride; an acid azide; a mixed acid anhydride with an acid such as substituted phosphoric acid [e.g. dialkylphosphoric acid, phenylphosphoric acid, diphenylphosphoric acid, dibenzylphosphoric acid, halogenated phosphoric acid, etc.], dialkylphosphorous acid, sulfurous acid, thiosulfuric acid, sulfuric acid, sulfonic acid [e.g. methanesulfonic acid, etc.], aliphatic carboxylic acid [e.g. acetic acid, propionic acid, butyric acid, isobutyric acid, pivalic acid, pentanoic acid, isopentanoic acid, 2-ethylbutyric acid, trichloroacetic acid, etc.] or aromatic carboxylic acid [e.g. benzoic acid, etc.]; a symmetrical acid anhydride; an activated amide with imidazole, 4-substituted imidazole, dimethylpyrazole, triazole or tetrazole; or an activated ester [e.g. cyanomethyl ester, methoxymethyl ester, dimethyliminomethyl [$(CH_3)_2N{=}CH$-] ester, vinyl ester, propargyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester, trichlorophenyl ester, pentachlorophenyl ester, mesylphenyl ester, phenylazophenyl ester, phenyl thioester, p-nitrophenyl thioester, p-cresyl thioester, carboxymethyl thioester, pyranyl ester, pyridyl ester, piperidyl ester, 8-quinolyl thioester, etc.] or an ester with an N-hydroxy compound [e.g. N,N-dimethylhydroxylamine, 1-hydroxy-2-(1H)-pyridone, N-hydroxysuccinimide, N-hydroxyphthalimide, 1-hydroxy-IH-benzotriazole, etc.], and the like. These reactive derivatives can optionally be selected from them according to the kind of the compound (III) to be used.

[0058] The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, etc.], acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction. These conventional solvents may also be used in a mixture with water.

[0059] In this reaction, when the compound (III) is used in a free acid form or its salt form, the reaction is preferably

carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide; N-cyclohexyl-N'-morpholinoethylcarbodiimide; N-cyclohexyl-N'-(4-diethylaminocyclohexyl)carbodiimide; N,N'-diethylcarbodiimide, N,N'-diisopropylcarbodiimide; N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide; N,N'-carbonylbis-(2-methylimidazole); pentamethyleneketene-N-cyclohexylimine; diphenylketene-N-cyclohexylimine; ethoxyacetylene; 1-alkoxy-1-chloroethylene; trialkyl phosphite; ethyl polyphosphate; isopropyl polyphosphate; phosphorus oxychloride (phosphoryl chloride); phosphorus trichloride; diphenylphosphoryl azide; diphenyl chlorophosphate; diphenylphosphinic chloride; thionyl chloride; oxalyl chloride; lower alkyl haloformate [e.g. ethyl chloroformate, isopropyl chloroformate, etc.]; triphenylphosphine; 2-ethyl-7-hydroxybenzisoxazolium salt; 2-ethyl-5-(m-sulfophenyl)isoxazolium hydroxide intramolecular salt; 1-(p-chlorobenzenesulfonyloxy)-6-chloro-1H-benzotriazole; so-called Vilsmeier reagent prepared by the reaction of N,N-dimethylformamide with thionyl chloride, phosgene, trichloromethyl chloroformate, phosphorus oxychloride, etc.; or the like.

[0060] The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal bicarbonate, tri(lower)alkylamine, pyridine, 4-dimethylaminopyridine, N-(lower)alkylmorpholine, N,N-di(lower)alkylbenzylamine, or the like.

[0061] The reaction temperature is not critical, and the reaction is usually carried out under cooling to heating.

Process 2

[0062] The object compound (I) or its salt can be prepared by reacting a compound (IV) or its salt with a compound (V) or its reactive derivative at the carboxy group or a salt thereof.

[0063] Suitable salts of the compounds (IV) and (V) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0064] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

Process 3

[0065] The object compound (Ic) or its salt can be prepared by subjecting a compound (Ib) or its salt to deesterification reaction.

[0066] Suitable salt of the compound (Ic) may be the same as those exemplified for the compound (I).

[0067] Suitable salt of the compound (Ib) may be an acid addition salt as exemplified for the compound (I).

[0068] The reaction is carried out in accordance with a conventional method such as hydrolysis, reduction or the like.

[0069] The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid. Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. lithium, sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, 1,4-diazabicyclo [2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, or the like. Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, etc.] and Lewis acid [e.g. boron tribromide, etc.].

[0070] The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], xylene, diethylene glycol monomethyl ethyl, methylene chloride, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent.

[0071] The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

[0072] The reduction can be applied preferably for elimination of the ester moiety such as 4-nitrobenzyl, 2-iodoethyl, 2,2,2-trichloroethyl, or the like. The reduction method applicable for the elimination reaction may include chemical reduction and catalitic reduction.

[0073] Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.].

[0074] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Raney copper, Ullman copper, etc.] or the like.

[0075] The reduction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, an alcohol [e.g. methanol, ethanol, propanol, etc.], N,N-dimethylformamide, or a mixture thereof. Addi-

tionally, in case that the above-mentioned acids to be used in chemical reduction are in liquid, they can also be used as a solvent. Further, a suitable solvent to be used in catalytic reduction may be the above-mentioned solvent, and other conventional solvent such as diethyl ether, dioxane, tetrahydrofuran, etc., or a mixture thereof.

[0076] The reaction temperature of this reduction is not critical and the reaction is usually carried out under cooling to warming.

[0077] In this reaction, in case that the compound (Ib) having lower alkyl substituted with esterified carboxy for R^2 and/or acyloxy, lower alkoxy substituted with esterified carboxy, lower alkylthio substituted with esterified carboxy, or lower alkyl substituted with esterified carboxy for R^4 is used as a starting compound, the compound (Ic) having lower alkyl substituted with carboxy for R^2 and/or hydroxy, lower alkoxy substituted with carboxy, lower alkylthio substituted with carboxy, or lower alkyl substituted with carboxy for R^4 may be obtained according to reaction condition. This case is included within the scope of this reaction.

Process 4

[0078] The object compound (Ie) or its salt can be prepared by subjecting a compound (Id) or its salt to deesterification reaction.

[0079] Suitable salt of the compound (Id) may be an acid addition salt as exemplified for the compound (I).

[0080] Suitable salt of the compound (Ie) may be the same as those exemplified for the compound (I).

[0081] This reaction can be carried out in substantially the same manner as hydrolysis in Process 3, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in hydrolysis in Process 3.

[0082] In this reaction, in case that the compound (Id) having aryl, haloaryl, cyclo(lower)alkyl or a heterocyclic group, each of which is substituted with esterified carboxy; lower alkenyl substituted with esterified carboxy; lower alkyl substituted with esterified carboxy, esterified carboxy(lower)alkanoyloxy or esterified carboxy(lower)alkoxyimino; lower alkylthio substituted with esterified carboxy; alkoxy substituted with esterified carboxy-substituted aryl, esterified carboxy-substituted pyridyl, esterified carboxy(lower)alkylamino, N-protected-esterified carboxy(lower)alkylamino, N-esterified carboxy(lower)alkyl-N-lower alkylamino, esterified carboxy or esterified carboxy(lower)alkoxyimino; or lower alkenyloxy substituted with esterified carboxy for R^1 and/or lower alkyl substituted with esterified carboxy for R^2 is used as a starting compound, the compound (Ie) having aryl, haloaryl, cyclo(lower)alkyl or a heterocyclic group, each of which is substituted with carboxy; lower alkenyl substituted with carboxy; lower alkyl substituted with carboxy, carboxy (lower)alkanoyloxy or carboxy(lower)alkoxyimino; lower alkylthio substituted with carboxy; alkoxy substituted with carboxy-substituted aryl, carboxy-substituted pyridyl, carboxy(lower)-alkylamino, N-protected-carboxy(lower)alkylamino, N-carboxy(lower)alkyl-N-lower alkylamino, carboxy or carboxy(lower)alkoxyimino; or lower alkenyloxy substituted with carboxy for R^1 and/or lower alkyl substituted with carboxy for R^2 may be obtained according to reaction condition. This case is included within the scope of this reaction.

Process 5

[0083] The object compound (Ig) or its salt can be prepared by subjecting a compound (If) or its salt to elimination reaction of the N-protective group.

[0084] Suitable salts of the compounds (If) and (Ig) may be acid addition salts as exemplified for the compound (I).

[0085] This reaction is carried out in accordance with a conventional method such as hydrolysis, reduction or the like.

[0086] The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid.

[0087] Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, hydrazine, alkylamine [e.g. methylamine, trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0] non-5-ene, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, or the like.

[0088] Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, hydrogen fluoride, etc.] and an acid addition salt compound [e.g. pyridine hydrochloride, etc.].

[0089] The elimination using trihaloacetic acid [e.g. trichloroacetic acid, trifluoroacetic acid, etc.] or the like is preferably carried out in the presence of cation trapping agents [e.g. anisole, phenol, etc.].

[0090] The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], methylene chloride, chloroform, tetrachloromethane, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent. The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

[0091] The reduction method applicable for the elimination reaction may include chemical reduction and catalytic reduction.

[0092] Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.].

[0093] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalysts [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalysts [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalysts [e.g. reduced cobalt, Raney cobalt, etc.], iron catalysts [e.g. reduced iron, Raney iron, etc.], copper catalysts [e.g. reduced copper, Raney copper, Ullman copper, etc.] and the like.

[0094] In case that the N-protective group is benzyl, the reduction is preferably carried out in the presence of a combination of palladium catalysts [e.g. palladium black, palladium on carbon, etc.] and formic acid or its salt [e.g. ammonium formate, etc.].

[0095] The reduction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, methanol, ethanol, propanol, N,N-dimethylformamide, or a mixture thereof. Additionally, in case that the above-mentioned acids to be used in chemical reduction are in liquid, they can also be used as a solvent. Further, a suitable solvent to be used in catalytic reduction may be the above-mentioned solvent, and other conventional solvent such as diethyl ether, dioxane, tetrahydrofuran, etc. or a mixture thereof.

[0096] The reaction temperature of this reduction is not critical and the reaction is usually carried out under cooling to heating.

[0097] In this reaction, in case that the compound (If) having aryl which is substituted with alkoxy substituted with protected amino, N-protected amino(lower)alkanoylamino, N-protected piperazinylcarbonyl or N-protected guanidino for R^1 is used as a starting compound, the compound (Ig) having aryl which is substituted with alkoxy substituted with amino, amino(lower)alkanoylamino, piperazinylcarbonyl or guanidino for R^1 may be obtained according to reaction condition. This case is included within the scope of this reaction.

Process 6

[0098] The object compound (Ih) or its salt can be prepared by reacting a compound (Ic) or its reactive derivative at the carboxy group or a salt thereof with an amine or its salt.

[0099] Suitable salt of amine may be an acid addition salt as exemplified for the compound (I).

[0100] Suitable salts of the compounds (Ih) and (Ic) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0101] Suitable "amine" may be ammonia, substituted or unsubstituted lower alkylamine, substituted or unsubstituted N-containing heterocyclic compound, a heterocyclic group substituted with amino and the like.

[0102] The substituted or unsubstituted lower alkylamine may be mono or di(lower)alkylamine (e.g. methylamine, ethylamine, propylamine, isopropylamine, butylamine, isobutylamine, pentylamine, hexylamine, dimethylamine, diethylamine, dipropylamine, dibutylamine, di-isopropylamine, dipentylamine, dihexylamine, etc.), pyridyl(lower) alkylamine, (e.g. pyridylmethylamine, etc.), lower alkylamino(lower)alkylamine (e.g. N-dimethylaminoethylamine, N-dimethylaminopropylamine, N-diethylaminoethyl-N-methylamine, etc.), morpholino(lower)alkylamine (e.g. morpholinoethylamine, etc.) or the like.

[0103] The substituted or unsubstituted N-containing heterocyclic compound may be a heterocyclic group substituted with amino (e.g. aminopyridine, N-methyl-N'-aminopiperazine, etc.), saturated 5 or 6-membered N-, or N- and S-, or N- and O-containing heterocyclic compound such as pyrrolidine, imidazolidine, piperidine, piperidone, piperazine, lower alkylaminopiperidine (e.g. dimethylaminopiperidine, etc.), N-(lower)alkylhomopiperazine (e.g. N-methylhomopiperazine, etc.), N-(lower)alkylpiperazine (e.g. N-methylpiperazine, N-ethylpiperazine, etc.), morpholine, thiomorpholine, N-pyridylpiperazine, N-hydroxy(lower)alkoxy(lower)-alkylpiperazine (e.g. N-hydroxyethoxyethylpiperazine, etc.), N-pyrrolidinylcarbonyl(lower)alkylpiperazine (e.g. N-pyrrodidinylcarbonylmethylpiperazine, etc.), or the like, in which preferable one is N-methylpiperazine.

[0104] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

Process 7

[0105] The object compound (Ii) or its salt can be prepared by reacting a compound (Ie) or its reactive derivative at the carboxy group or a salt thereof with an amine or its salt.

[0106] Suitable salt of amine may be an acid addition salt as exemplified for the compound (I).

[0107] Suitable salts of the compounds (Ii) and (Ie) and its reactive derivative at the carboxy group may be the same

as those exemplified for the compound (I).

[0108] This reaction can be carried out in substantially the same manners as Processes 1 and 6, and therefore the reaction mode and reaction condition (e.g. amine, solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Processes 1 and 6.

Process 8

[0109] The object compound (Ik) or its salt can be prepared by subjecting a compound (Ij) or its salt to debenzylation reaction.

[0110] Suitable salts of the compounds (Ij) and (Ik) may be the same as those exemplified for the compound (I).

[0111] This reaction can be carried out in substantially the same manner as hydrolysis using an acid or catalytic reduction in Process 5, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in hydrolysis using an acid or catalylic reduction in Process 5.

[0112] In this catalytic reduction, in case that the compound (Ij) having nitro for R^3 is used as a starting compound, the compound (Ik) having amino for R^3 may be obtained according to reaction condition. This case is included within the scope of this reaction.

Process 9

[0113] The object compound (Il) or its salt can be prepared by reacting a compound (Ika) or its salt with a compound (VI) or its salt.

[0114] Suitable salts of the compounds (Ika), (Il) and (VI) may be the same as those exemplified for the compound (I).

[0115] When the compound (VI) having halogen for Z^1 is used in this reaction, the reaction is preferably carried out in the presence of a base such as an alkali metal (e.g. sodium, potassium, etc.), an alkaline earth metal (e.g. magnesium, calcium, etc.), the hydride or hydroxide or carbonate or bicarbonate thereof.

[0116] When the compound (VI) having hydroxy for Z^1 is used in this reaction, the reaction is preferably carried out in the presence of diethyl azodicarboxylate and triphenylphosphine.

[0117] The reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, dioxane, alcohol (e.g. methanol, ethanol, etc.), acetonitrile, tetrahydrofuran, acetic acid, N,N-dimethylformamide, or a mixture thereof.

[0118] The reaction temperature is not critical and the reaction can be carried out under cooling to heating.

Process 10

[0119] The object compound (Im) or its salt can be prepared by reacting a compound (Iga) or its salt with an acylating agent.

[0120] Suitable salts of the compounds (Iga) and (Im) may be the same as those exemplified for the compound (I).

[0121] The acylating agent may include an organic acid represented by the formula : R^{11}-OH, in which R^{11} is acyl or substituted acyl as illustrated above, or its reactive derivative.

[0122] The suitable reactive derivative of organic acid may be a conventional one such as an acid halide [e.g. acid chloride, acid bromide, etc.], an acid azide, an acid anhydride containing intramolecular and intermolecular ones, an activated amide, an activated ester or the like.

[0123] When free acid is used as an acylating agent, the acylation reaction may preferably be conducted in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide or the like.

[0124] The reaction is usually carried out in a conventional solvent such as water, pyridine, acetone, dioxane, chloroform, methylene chloride, acetonitrile, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction, or a mixture thereof.

[0125] The reaction is also preferably carried out in the presence of a conventional base such as triethylamine, pyridine, sodium hydroxide or the like.

[0126] The reaction temperature is not critical, and the reaction can be carried out under cooling to heating.

Process 11

[0127] The object compound (In) or its salt can be prepared by reacting a compound (Igb) or its salt with lower alkanal or N-protected amino(lower)alkanal in the presence of a reducing agent.

[0128] Suitable salts of the compounds (Igb) and (In) may be the same as those exemplified for the compound (I).

[0129] Suitable lower alkanal may be C_1-C_6 alkanal such as formaldehyde, ethanal, propanal or the like, in which

preferable one is formaldehyde.

[0130] Suitable N-protected amino(lower)alkanal may be N-protected amino(C_1-C_6)alkanal such as phthalimidopropanal or the like.

[0131] Suitable reducing agent may be diborane, borane-organic amine complex [e.g. borane-pyridine complex, etc.], alkali metal cyanoborohydride [e.g. sodium cyanoborohydride, lithium cyanoborohydride, etc.], sodium borohydride and the like.

[0132] The reaction is preferably carried out in the presence of molecular sieves.

[0133] The reaction is usually carried out in a conventional solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], dioxane, tetrahydrofuran, a mixture thereof or any other organic solvent which does not adversely influence the reaction.

[0134] The reaction may also be carried out in an acidic condition [e.g. presence of acetic acid, sulfuric acid, etc.] and the reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

Process 12

[0135] The object compound (Ip) or its salt can be prepared by subjecting a compound (Io) or its salt to reduction.

[0136] Suitable salts of the compounds (Io) and (Ip) may be the same as those exemplified for the compound (I).

[0137] The reduction may include chemical reduction and catalytic reduction, which are carried out in a conventional manner.

[0138] Suitable reducing agents to be used in chemical reduction are a metal [e.g. thin, zinc, iron, nickel, etc.], a combination of such metal and/or metallic compound [e.g. nickel chloride, chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.], a combination of such metal and/or metallic compound and base [e.g. ammonia, ammonium chloride, sodium hydroxide, etc.], a metal hydride compound such as aluminum hydride compound [e.g. lithium aluminum hydride, sodium aluminum hydride, aluminum hydride, lithium trimethoxyaluminum hydride, lithium tri-t-butoxyaluminum hydride, etc.], borohydride compound [e.g. sodium borohydride, lithium borohydride, sodium cyanoborohydride, tetramethylammonium borohydride, borane, diborane, etc.], a phosphorus compound [e.g. phosphorus trichloride, phosphorus tribromide, triphenylphosphine, triethylphosphine, etc.] and the like.

[0139] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Raney copper, Ullman copper, etc.], or the like.

[0140] The reduction is usually carried out in a solvent. A suitable solvent to be used may be water, and alcohol [e.g. methanol, ethanol, propanol, etc.], acetonitrile or any other conventional organic solvent such as diethyl ether, dioxane, tetrahydrofuran, etc. or a mixture thereof.

[0141] The reaction temperature is not critical, and the reaction is preferably carried out under cooling to heating.

Process 13

[0142] The object compound (Ir) or its salt can be prepared by subjecting a compound (Iq) or its salt to deacylation reaction.

[0143] Suitable salts of the compounds (Iq) and (Ir) may be the same as those exemplified for the compound (I).

[0144] This reaction can be carried out in substantially the same manner as Process 3, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 3.

Process 14

[0145] The object compound (Is) or its salt can be prepared by reacting a compound (VII) or its salt with a compound (VIII) or its salt.

[0146] Suitable salts of the compounds (Is), (VII) and (VIII) may be the same as those exemplified for the compound (I).

[0147] This reaction can be carried out in substantially the same manner as Process 9, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 9.

Process 15

[0148] The object compound (Iu) or its salt can be prepared by reacting a compound (It) or its salt with an oxidizing agent.

[0149] Suitable salts of the compounds (It) or (Iu) may be the same as those exemplified for the compound (I).

[0150] The suitable oxidizing agent may be hydrogen peroxide, Jones reagent, peracid [e.g. peracetic acid, perbenzoic acid, m-chloroperbenzoic acid, etc.], chromic acid, potassium permanganate, alkali metal periodate [e.g. sodium periodate, etc.] and the like.

[0151] This reaction is usually carried out in a solvent which does not adversely influence the reaction such as acetic acid, dichloromethane, acetone, ethyl acetate, chloroform, water, an alcohol [e.g. methanol, ethanol, etc.], a mixture thereof or the like.

[0152] The reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

Process 16

[0153] The object compound (Iw) or its salt can be prepared by subjecting a compound (Iv) or its salt to catalytic reduction.

[0154] Suitable salts of the compounds (Iv) and (Iw) may be the same as those exemplified for the compound (I).

[0155] This reaction can be carried out in substantially the same manner as catalytic reduction in Process 5, and threfore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in catalytic reduction in Process 5.

Process 17

[0156] The object compound (Iy) or its salt can be prepared by subjecting a compound (Ix) or its salt to debenzylation reaction.

[0157] Suitable salts of the compounds (Ix) and (Iy) may be the same as those exemplified for the compound (I).

[0158] This reaction can be carried out in substantially the same manner as Process 8, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 8.

Process 18

[0159] The object compound (Iz) or its salt can be prepared by reacting a compound (Iy) or its salt with a compound (IX) or its salt.

[0160] Suitable salts of the compounds (Iy), (Iz) and (IX) may be the same as those exemplified for the compound (I).

[0161] This reaction can be carried out in substantially the same manner as Process 9, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 9.

Process 19

[0162] The object compound (I-2) or its salt can be prepared by subjecting a compound (I-1) or its salt to elimination reaction of the hydroxy protective group.

[0163] Suitable salts of the compounds (I-1) and (I-2) may be the same as those exemplified for the compound (I).

[0164] Suitable hydroxy protective group may be benzyloxy, acyloxy, substituted acyloxy or the like.

[0165] This reaction can be carried out in substantially the same manner as Processes 8 and 13, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Processes 8 and 13.

Process 20

[0166] The object compound (I-3) or its salt can be prepared by reacting a compound (I-2) or its salt with a compound (X) or its salt.

[0167] Suitable salts of the compounds (I-2), (I-3) and (X) may be the same as those exemplified for the compound (I).

[0168] This reaction can be carried out in substantially the same manner as Process 9, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 9.

Process 21

[0169] The object compound (I-4) or its salt can be prepared by subjecting a compound (I-3a) or its salt to deesterification reaction.

[0170] Suitable salts of the compounds (I-3a) and (I-4) may be the same as those exemplified for the compound (I).

[0171] This reaction can be carried out in substantially the same manner as Process 3, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 3.

Process 22

[0172] The object compound (I-6) or its salt can be prepared by reacting a compound (I-5) or its salt with an alkyne compound in the presence of a palladium compound and a copper compound.

[0173] Suitable salts of the compounds (I-5) and (I-6) may be the same as those exemplified for the compound (I).

[0174] Suitable alkyne compound may be lower alkyne optionally substituted with hydroxy, amino, protected amino, lower alkylsulfonyl, arylsulfonyl or the like, in which preferable one is 3-butyn-1-ol.

[0175] Suitable palladium compound may be bis(triphenylphosphine)palladium(II) chloride, or the like.

[0176] Suitable copper compound may be copper(I) iodide, or the like.

[0177] The reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as tetrahydrofuran, dioxane, ethylamine, or a mixture thereof.

[0178] The reaction temperature is not critical and the reaction is usually carried out under warming or heating.

Process 23

[0179] The object compound (I-8a) or its salt can be prepared by reacting a compound (I-7) or its salt with a compound (XI).

[0180] Suitable salts of the compounds (I-7) and (I-8a) may be the same as those exemplified for the compound (I).

[0181] The reaction is preferably carried out in the presence of a base such as trialkylamine (e.g. trimethylamine, triethylamine, etc.) or the like.

[0182] The reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as tetrahydrofuran, methylene chloride or the like.

[0183] The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

Process 24

[0184] The object compound (I-9) or its salt can be prepared by reacting a compound (I-8) or its salt with alkali metal phthalimide.

[0185] Suitable salts of the compounds (I-8) and (I-9) may be the same as those exemplified for the compound (I).

[0186] The reaction is carried out in a conventional solvent which does not adversely influence the reaction such as dimethyl sulfoxide, N,N-dimethylformamide, or the like.

[0187] The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

Process 25

[0188] The object compound (I-10) or its salt can be prepared by reacting a compound (I-6) or its salt with a reducing agent.

[0189] Suitable salts of the compounds (I-6) and (I-10) may be the same as those exemplified for the compound (I).

[0190] Suitable reducing agent may be a combination of nickel chloride and sodium borohydride, and the like.

[0191] The reaction is carried out in a conventional solvent which does not adversely influence the reaction such as an alcohol (e.g. methanol, ethanol, etc.), tetrahydrofuran, or a mixture thereof.

[0192] The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

Process 26

[0193] The object compound (I-11) or its salt can be prepared by reacting a compound (II) or its salt with a compound (XII) or its salt.

[0194] Suitable salts of the compounds (I-11), (II) and (XII) may be the same as those exemplified for the compound (I).

[0195] This reaction can be carried out in substantially the same manner as Process 11, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 11.

Process 27

[0196] The object compound (I-13) or its salt can be prepared by reacting a compound (I-12) or its salt with a compound (XIII) in the presence of a base.

[0197] Suitable salts of the compounds (I-12) and (I-13) may be the same as those exemplified for the compound (I).

[0198] Suitable base may be an alkali metal (e.g. sodium, potassium, etc.), an alkali metal hydride (e.g. sodium hydride), and the like.

[0199] The reaction is carried out in a solvent such as N,N-dimethylformamide, tetrahydrofuran, dioxane, a mixture thereof or any other solvent which does not adversely influence the reaction.

[0200] The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

Process 28

[0201] The object compound (I-15) or its salt can be prepared by reacting a compound (I-14) or its salt with an acylating agent.

[0202] Suitable salts of the compounds (I-14) and (I-15) may be the same as those exemplified for the compound (I).

[0203] This reaction can be carried out in substantially the same manner as Process 10, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 10.

Process 29

[0204] The object compound (I-17) or its salt can be prepared by reacting a compound (I-16a) or its salt with a reducing agent.

[0205] Suitable salts of the compounds (I-16a) and (I-17) may be the same as those exemplified for the compound (I).

[0206] Suitable reducing agent may be alkali metal borohydride (e.g. sodium borohydride, etc.), and the like.

[0207] The reaction is carried out in a solvent such as an alcohol (e.g. methanol, ethanol, etc.), tetrahydrofuran, or the like.

[0208] The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

Process 30

[0209] The object compound (I-18) or its salt can be prepared by reacting a compound (I-16) or its salt with an amine compound or its salt in the presence of a reducing agent.

[0210] Suitable salts of the compounds (I-16) and (I-18) may be the same as those exemplified for the compound (I).

[0211] Suitable amine compound may be ammonia, N-lower alkylpiperazine, and the like.

[0212] Suitable salt of amine compound may be an acid addition salt (e.g. acetate, hydrochloride, etc.), and the like.

[0213] This reaction can be carried out in substantially the same manner as Process 11, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 11.

Process 31

[0214] The object compound (I-20) or its salt can be prepared by reacting a compound (I-19) or its reactive derivative at the carboxy group or a salt thereof with lower alkylamino(lower)alkanol.

[0215] Suitable salts of the compounds (I-20) and (I-19) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0216] Suitable lower alkylamino(lower)alkanol may be dimethylaminoethanol, and the like.

[0217] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

Process 32

[0218] The object compound (I-22) or its salt can be prepared by reacting a compound (I-21) or its salt with a reducing agent.

[0219] Suitable salts of the compounds (1-21) and (I-22) may be the same as those exemplified for the compound (I).

[0220] Suitable reducing agent may be diborane, lithium aluminum hydride and the like.

[0221] The reaction is usually carried out in a solvent which does not adversely influence the reaction such as diethyl ether, tetrahydrofuran or the like.

[0222] The reaction temperature is not critical and the reaction can be carried out under cooling to heating.

Process 33

[0223] The object compound (I-23) or its salt can be prepared by subjecting a compound (I-22) or its salt to oxidation reaction.

[0224] Suitable salts of the compounds (I-22) and (I-23) may be the same as those exemplified for the compound (I).

[0225] Suitable oxidizing agent used in this reaction may be manganese dioxide, dimethyl sulfoxide, a mixture of dimethyl sulfoxide and oxalyl chloride and the like.

[0226] The reaction is usually carried out in a conventional solvent such as pentane, hexane, benzene, diethyl ether, dimethoxyethane, acetone, chloroform, dichloromethane or any other solvent which does not adversely influence the reaction.

[0227] Additionally in case that the above-mentioned oxidizing agent is liquid, it can be used as a solvent.

[0228] In this reaction, in case that dimethyl sulfoxide or a mixture of dimethyl sulfoxide and oxalyl chloride is used as an oxidizing agent, the reaction is preferably carried out in the presence of alkali metal iodide (e.g. sodium iodide, etc.) and alkali metal carbonate (e.g. sodium carbonate) or tri(lower)alkylamine (e.g. triethylamine, etc.).

[0229] The reaction temperature is not critical, and the reaction is usually carried out under cooling to heating.

Process 34

[0230] The object compound (I-25) or its salt can be prepared by reacting a compound (I-24) or its salt with an azide compound.

[0231] Suitable salts of the compounds (I-24) and (I-25) may be the same as those exemplified for the compound (I).

[0232] Suitable azide compound may be sodium azide, trimethyltin azide and the like.

[0233] The reaction is usually carried out in a solvent which does not adversely influence the reaction such as dioxane, an aromatic hydrocarbon (e.g. benzene, toluene, xylene) or the like.

[0234] The reaction temperature is not critical and the reaction is usually carried out under warming to heating.

Process 35

[0235] The object compound (I-27) or its salt can be prepared by reacting a compound (I-26) or its salt with an isourea compound.

[0236] Suitable salts of the compounds (I-26) and (I-27) may be the same as those exemplified for the compound (I).

[0237] Suitable isourea compound may be O-alkylisourea (e.g. O-methylisourea, etc.) and the like.

[0238] The reaction is usually carried out in a solvent which does not adversely influence the reaction such as an alcohol (e.g. methanol, ethanol, etc.) or the like.

[0239] The reaction temperature is not critical and the reaction is usually carried out under warming to heating.

Process 36

[0240] The object compound (I-29) or its salt can be prepared by subjecting a compound (I-28) or its salt to elimination reaction of the N-protective group.

[0241] Suitable salts of the compounds (I-28) and (I-29) may be the same as those exemplified for the compound (I) .

[0242] This reaction can be carried out in substantially the same manner as Process 5, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 5.

Process 37

[0243] The object compound (I-31) or its salt can be prepared by reacting a compound (I-30) or its salt with N-lower

alkylpiperazine, dimethylaminopiperidine, ammonia or N,N-dimethylformamide.

[0244] Suitable salts of the compounds (I-30) and (I-31) may be the same as those exemplified for the compound (I).

[0245] The reaction is usually carried out in a solvent which does not adversely influence the reaction such as N,N-dimethylformamide, dioxane or the like.

[0246] The reaction temperature is not critical and the reaction is usually carried out under warming to heating.

Process 38

[0247] The object compound (I-3a) or its salt can be prepared by reacting a compound (I-4) or its reactive derivative at the carboxy group or a salt thereof with a hydroxy compound or a diazo compound.

[0248] Suitable salts of the compounds (I-3a) and (I-4) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0249] Suitable reactive derivative at the carboxy group (I-4) may be acid halide (e.g. acid chloride, acid bromide, etc.) and the like.

[0250] Suitable hydroxy compound may be an alcohol (e.g. methanol, ethanol, etc.), phenol, naphthol and the like.

[0251] Suitable diazo compound may be methyldiazomethane, trimethylsilyldiazomethane and the like.

[0252] The reaction is usually carried out in a conventional solvent such as diethyl ether, tetrahydrofuran, dioxane, methylene chloride, or any other organic solvent which does not adversely influence the reaction.

[0253] Additionally, in case that the above-mentioned hydroxy compound is in liquid, it can also be used as a solvent.

[0254] The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

Process 39

[0255] The object compound (I-32) or its salt can be prepared by reacting a compound (I-4) or its reactive derivative at the carboxy group or a salt thereof with an amine.

[0256] Suitable salts of the compounds (I-32) and (I-4) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0257] Suitable amine may be ammonia, lower alkylamine (e.g. methylamine, dimethylamine, etc.) and the like.

[0258] This reaction can be carried out in substantially the same manner as Process 6, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 6.

[0259] The compounds obtained by the above processes can be isolated and purified by a conventional method such as pulverization, recrystallization, column chromatography, reprecipitation, or the like.

[0260] It is to be noted that the compound (I) and the other compounds may include one or more stereoisomer(s) such as optical isomer(s) or geometrical isomer(s) due to asymmetric carbon atom(s) and double bond(s), and all of such isomers and mixture thereof are included within the scope of this invention.

[0261] Additionally, it is to be noted that any hydrate of the compound (I) is also included within the scope of this invention.

[0262] The object compound (I) and pharmaceutically acceptable salts thereof possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity, oxytocin antagonistic activity and the like, and are useful for the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, cerebrovascular disease (e.g. cerebral edema, cerebral infarction, etc.), Meniere's syndrome (e.g. Meniere's disease, et.), motion sickness and the like in human beings and animals.

[0263] In order to illustrate the usefulness of the object compound (I), the pharmacological data of the compound (I) are shown in the following.

Test 1

[0264] Vasopressin 1 (V1) receptor binding

(i) Test Method :

[0265] Blood was obtained by venipuncture from normal subjects. Platelet-rich plasma (PRP) was prepared by centrifugation of whole blood at 200 xg for 10 minutes. PRP was centrifuged at 45,000 xg for 30 minutes. The remaining pellet was resuspended in 10 volume of ice cold 100 mM Tris-HCl (pH 7.4) buffer (containing 5 mM $MgCl_2$, 0.1% bovine serum albumin and 1 mM EGTA), and centrifuged at 45,000 xg for 30 minutes again. The final pellet was resuspended

in 100 mM Tris-HCl buffer. The resulting membrane preparation was used immediately for the binding assay.

[0266] Competition assays were conducted at equilibrium (15 minutes at 30°C) by using 1.5 nM ^{3}H-vasopressin (40-87 Ci/mmol; New England Nuclear) in 100 mM Tris-HCl (pH 7.4) buffer. Nonspecific binding was determined by using 1 μM vasopressin. After incubation, reaction was terminated by adding 5 ml of ice-cold 100 mM Tris-HCl (pH 7.4) buffer, and then filtered rapidly through Whatman glass filter (GF/C). The filter was washed twice with the same buffer. The glass filter was mixed with liquid scintilation cocktail, and radioactivity was counted in a liquid scintilation counter. Competition activity of the test compound was represented by IC_{50} values.

(ii) Test Result :

[0267]

Test Compound (Example No.)	IC_{50} (nM)
5-2)	51
16	14
17-20)	31

Test 2

[0268] Vasopressin 2 (V2) receptor binding

(i) Test Method :

[0269] For binding assays, the receptor cDNA was permanently expressed in Chinese hamster ovary (CHO) cells. CHO cells were transfected with a vector directing expression of the cDNA for the human V2 receptor and the clonal cell lines expressing human V2 receptor was established essentially as described previously (Nakajima, Y., et. al. J. Biol. Chem., 1992, 267, 2437).

[0270] DNA-transfected cells were harvested and homogenized in ice cold 250 mM sucrose buffer containing 25 mM Tris-HCl (pH 7.4), 10 mM $MgCl_2$, 1 mM EDTA and 5 μg/ml p-amidinophenylmethylsulfonyl fluoride (A-PMSF). The homogenate was centrifuged at 500 xg for 10 minutes. The supernatant was centrifuged at 100,000 xg for 1 hour. The final pellet was suspended in 25 mM Tris-HCl (pH 7.4) buffer (containing 10 mM $MgCl_2$, 1 mM EDTA and 5 μg/ml A-PMSF), and stored in small aliquots at -80°C.

[0271] Competition assays were conducted at equilibrium (2 hours at 22°C) by using 0.5 nM ^{3}H-vasopressin (40-87 Ci/mmol, New England Nuclear) in 100 mM Tris-HCl (pH 7.4) buffer (containing 5 mM $MgCl_2$, 5 μg/ml A-PMSF, 4 μg/ml leupeptin, 40 μg/ml bacitracin, 20 μg/ml chymostatin and 0.1% bovine serum albumin). Nonspecific binding was determined by using 1 μM vasopressin. After incubation, reaction mixture was rapidly filtered through Whatman glass filter (GF/C). The filter was washed twice with the same buffer. The radioactivity was counted in a liquid scintilation counter. Competition activity of the test compound was represented by IC_{50} values.

(ii) Test Result :

[0272]

Test Compound (Example No.)	IC_{50} (nM)
5-2)	1300
16	1400
17-20)	1300

[0273] For therapeutic purpose, the compound (I) of the present invention can be used in a form of pharmaceutical preparation containing one of said compounds, as an active ingredient, in admixture with a pharmaceutically acceptable carrier such as an organic or inorganic solid, semi-solid or liquid excipient suitable for oral, parenteral or external (topical) administration. The pharmaceutical preparations may be capsules, tablets, dragees, granules, suppositories, solution, lotion, suspension, emulsion, ointment, gel, or the like. If desired, there may be included in these preparations, auxiliary substances, stabilizing agents, wetting or emulsifying agents, buffers and other commonly used additives.

[0274] While the dosage of the compound (I) will vary depending upon the age and condition of the patient, an average single dose of about 0.1 mg, 1 mg, 10 mg, 50 mg, 100 mg, 250 mg, 500 mg and 1000 mg of the compound (I) may be effective for treating the above-mentioned diseases. In general, amounts between 0.1 mg/body and about 1,000 mg/body may be administered per day.

[0275] The following Preparations and Examples are given for the purpose of illustrating this invention.

Preparation 1

[0276] To a solution of [N-methyl-N-(4-nitrobenzoyl]-2-hydroxyaniline (1.2 g) in N,N-dimethylformamide (30 ml) was added potassium carbonate (1.22 g), ethyl 6-bromohexanoate (1.03 g) and sodium iodide (catalytic amount) at 60°C. The reaction mixture was stirred at same temperature for 8 hours. The reaction mixture was cooled in an ice bath and quenched with 1N hydrochloric acid (10 ml) and water (30 ml). The mixture was extracted with ethyl acetate. The organic phase was washed with water and brine. The organic solution was dried over magnesium sulfate. The solvent was removed by evaporation to give 2-(5-ethoxycarbonylpent-1-yloxy)-[N-methyl-N-(4-nitrobenzoyl)]aniline (1.7 g).

NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 1.45-1.58 (2H, m), 1.67-1.76 (2H, m), 1.79-1.88 (2H, m), 2.34 (2H, t, J=7.5Hz), 3.38 (3H, s), 3.84-4.00 (2H, m), 4.13 (2H, t), 6.72-6.82 (2H, m), 7.01 (1H, d, J=7Hz), 7.17 (1H, t, J=7Hz), 7.45 (2H, d, J=8.5Hz), 7.98 (2H, d, J=8.5Hz)

Preparation 2

[0277] A solution of 3-methoxy-4-nitro-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]-N-methylbenzamide (7.6 g) in ethanol (76 ml) was treated with 1N sodium hydroxide solution (33 ml) at ambient temperature and the mixture was stirred at the same temperature for 6 hours. The reaction was quenched by the dropwise addition of 1N hydrochloric acid (35 ml). The mixture was concentrated and the residue was dissolved in a mixture of ethyl acetate and 1N hydrochloric acid. The extracted organic layer was washed with brine and dried over magnesium sulfate. The suspension was filtered and the solvent was removed by evaporation to give 3-methoxy-4-nitro-N- [2-(5-carboxypent-1-yloxy)-4-methylphenyl]-N-methylbenzamide (7.1 g) as an oil.

NMR ($CDCl_3$, δ) : 1.48-1.63 (2H, m), 1.66-1.91 (4H, m), 2.28 (3H, s), 2.41 (2H, t, J=7Hz), 3.34 (3H, s), 3.78 (3H, s), 3.81-3.98 (2H, m), 6.58-6.67 (2H, m), 6.89 (1H, d, J=8Hz), 6.94 (1H, d, J=8Hz), 7.09 (1H, s), 7.61 (1H, d, J=8Hz)

Preparation 3

[0278] 3-Methoxy-4-nitro-N- [2- (5-carboxypent-1-yloxy)-4-methylphenyl]-N-methylbenzamide (5.2 g), 1-methylpiperazine (1.45 g) and 1-hydroxybenzotriazole (1.96 g) were dissolved in N,N-dimethylformamide (50 ml) and the solution was cooled in an ice bath. To the mixture was added N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride (2.78 g) and the solution was stirred at the same temperature for 30 minutes. The reaction mixture was allowed to warm to ambient temperature and stirring was continued for additional 20 hours. The reaction mixture was diluted with ethyl acetate and the solution was washed successively with saturated sodium hydrogen carbonate and brine, and dried over sodium sulfate. The sodium sulfate was removed and the solvent was removed by evaporation to give oil. The crude material was subjected to a silica gel column chromatography (SiO_2; 120 g, 2% methanol in chloroform) to give 3-methoxy-4-nitro-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]phenyl]benzamide (6.2 g) .

NMR ($CDCl_3$, δ) : 1.43-1.60 (2H, m), 1.60-1.92 (4H, m), 2.28 (3H, s), 2.30 (3H, s), 2.25-2.47 (6H, m), 3.34 (3H, s), 3.44-3.54 (2H, m), 3.58-3.70 (2H, m), 3.78 (3H, s), 3.82-4.03 (2H, m), 6.56-6.66 (2H, m), 6.86 (1H, d, J=8Hz), 6.94 (1H, d, J=8Hz), 7.07 (1H, s), 7.61 (1H, d, J=8Hz)

Preparation 4

[0279] A mixture of 3-methoxy-4-nitro-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy] phenyl]benzamide (6.2 g) and iron powder (3.43 g) in a mixture of ethanol (65 ml) and ethyl acetate (6 ml) was refluxed for 2 hours. After being cooled to ambient temperature, the solution was filtered through a bed of Celite and the filtrate was evaporated in vacuo. The residue was diluted with ethyl acetate and the solution was washed with saturated sodium hydrogen carbonate and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]phenyl]benzamide (4.7 g).

NMR ($CDCl_3$, δ) : 1.43-1.58 (2H, m), 1.61-1.91 (4H, m), 2.26 (3H, s), 2.30 (3H, s), 2.23-2.44 (6H, m), 3.29 (3H, s), 3.41-3.53 (2H, m), 3.61 (3H, s), 3.57-3.68 (2H, m), 3.75-4.03 (4H, m), 6.36-6.46 (1H, m), 6.53-6.67 (2H, m), 6.76-6.89 (3H, m)

Preparation 5

[0280] The following compounds were obtained according to a similar manner to that of Preparation 4.

1) 4-Amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)phenylbenzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 1.41-1.54 (2H, m), 1.62-1.73 (2H, m), 1.75-1.84 (2H, m), 2.32 (2H, t, J=7.5Hz), 3.30 (3H, s), 3.84 (2H, br), 3.90 (2H, br), 4.13 (2H, t), 6.38 (2H, d, J=8.5Hz), 6.79 (2H, d, J=8.5Hz), 6.99 (2H, s), 7.09-7.18 (3H, m)

2) 4-Amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl] benzamide
NMR ($CDCl_3$, δ) : 1.29-1.95 (10H, m), 2.23-2.43 (12H, m), 2.57 (1H, m), 3.01 (1H, m), 3.31 (3H, s), 3.62 (3H, s), 3.73-4.03 (5H, m), 4.63 (1H, m), 6.42 (1H, d, J=9Hz), 6.54-6.67 (2H, m), 6.77-6.89 (3H, m)

3) 4-Amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
MASS (m/z) : 399 (M+1)

4) 4-Amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.32 (3H, s), 2.35-2.55 (4H, m), 3.31 (3H, s), 3.38-3.54 (2H, m), 3.66-3.87 (4H, m), 4.90-5.10 (2H, m), 6.38 (2H, d, J=8Hz), 6.62-6.69 (2H, m), 6.94 (1H, d, J=7Hz), 7.13 (2H, d, J=8Hz), 7.31-7.43 (4H, m)

5) 2-(4-Methoxycarbonyl)phenylmethoxy-4-methylamine
NMR ($CDCl_3$, δ) : 2.24 (3H, s), 3.90 (3H, s), 5.11 (3H, s), 6.60-6.68 (3H, m), 7.50 (2H, d, J=8Hz), 8.05 (2H, d, J=8Hz)

6) 4-Amino-3-methoxy-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 2.33 (3H, s), 2.37-2.53 (4H, m), 3.36 (3H, s), 3.41-3.54 (2H, m), 3.57 (3H, s), 3.65-3.90 (4H, m), 4.90 (1H, d, J=14Hz), 5.06 (1H, d, J=14Hz), 6.38 (1H, d, J=7Hz), 6.62-6.70 (2H, m), 6.78 (1H, d, J=7Hz), 6.84 (1H, s), 6.98 (1H, d, J=7Hz), 7.33 (2H, d, J=8Hz), 7.41 (2H, d, J=8Hz)

7) Methyl 4-[(E and Z)-2-(2-aminophenyl)ethen-1-yl]benzoate
NMR ($CDCl_3$, δ) : 3.72 (2H, br), 3.86 (3Hx2/3, s), 3.90 (3Hx1/3, s), 6.57-7.43 (7H, m), 7.55 (1H, d, J=7Hz), 7.86 (1H, d, J=7Hz), 8.01 (7H, d)

8) 4-Amino-3-methoxy-N-[(E and Z) -2- (4-methoxycarbonylphenyl) ethen-1-yl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.39 (3Hx2/3, s), 3.40 (3Hx1/3, s), 3.50 (3Hx2/3, s), 3.51 (3Hx1/3, s), 3.81-3.96 (2H, m), 3.84 (3Hx2/3, s), 3.41 (3Hx1/3, s), 6.30-8.05 (13H, m)

9) 4-Amino-3-methoxy-N-[2- (4-methoxycarbonyl)-phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.21 (3H, s), 3.34 (3H, s), 3.50 (3H, s), 3.83 (2H, s), 3.90 (3H, s), 4.79-5.14 (2H, m), 6.37 (1H, d, J=7Hz), 6.60 (1H, s), 6.70 (1H, d, J=7Hz), 6.77 (1H, d, J=7Hz), 6.81 (1H, s), 6.99 (1H, d, J=7Hz), 7.34 (2H, d, J=8Hz), 8.01 (2H, d, J=8Hz)

10) 2-[3-(Ethoxycarbonylmethyl)oxyprop-1-yl]oxyaniline
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.08-2.28 (2H, m), 3.72 (2H, t, J=7.5Hz), 3.79 (2H, s), 4.09 (2H, s), 4.14 (2H, t, J=7.5Hz), 4.21 (2H, q, J=7.5Hz), 6.65-6.82 (4H, m)

11) 4-Amino-3-methoxy-N-[2-[3-(ethoxycarbonylmethyl)-oxyprop-1-yl]oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 2.03-2.15 (2H, m), 3.31 (3H, s), 3.61 (3H, s), 3.69-3.77 (4H, m), 4.02 (2H, s), 4.20 (2H, q, J=7.5Hz), 6.41 (1H, d, J=7.5Hz), 6.64-6.89 (4H, m), 7.00 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz)

12) 2-[(E)-5-Ethoxycarbonyl-4-penten-1-yl]oxy-4-methylaniline
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=7.5Hz), 1.90-2.05 (2H, m), 2.23 (3H, s), 2.35-2.50 (2H, m), 3.65 (2H, br), 4.00 (2H, t, J=7.5Hz), 4.18 (2H, q, J=7.5Hz), 5.98 (1H, d, J=15Hz), 6.53-6.67 (2H, m), 6.81 (1H, s), 7.00 (1H, dt, J=15, 7.5Hz)

13) 4-Amino-3-methoxy-N-[2-[(E)-5-ethoxycarbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 1.84-1.98 (2H, m), 2.36 (3H, s), 2.31-2.41 (2H, m), 3.29 (3H, s), 3.62 (3H,

s), 3.75-3.96 (4H, m), 4.18 (2H, q, J=7.5Hz), 5.84 (1H, d, J=15Hz), 6.40 (1H, d, J=7Hz), 6.58-6.63 (2H, m), 6.78-7.01 (4H, m)

14) 2-(5-Ethoxycarbonylpent-1-yloxy)-4-methylaniline
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.45-1.60 (2H, m), 1.63-1.89 (4H, m), 2.25 (3H, s), 2.33 (2H, t, J=7Hz), 3.98 (2H, t, J=7Hz), 4.13 (2H, q, J=7Hz), 6.54-6.68 (3H, m)

15) 3-Methoxy-4-amino-N-(2-benzyloxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 3.32 (3H, s), 3.49 (3H, s), 3.83 (2H, br), 4.80-5.11 (2H, br), 6.34 (1H, d, J=8Hz), 6.62-6.84 (5H, m), 6.92 (1H, d, J=8Hz), 7.25-7.39 (4H, m)

16) 4-Amino-3-methyl-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.59 (2H, m), 1.63-1.88 (4H, m), 2.00 (3H, s), 2.28 (3H, s), 2.30 (3H, s), 2.32-2.40 (6H, m), 3.29 (3H, s), 3.43-3.48 (2H, m), 3.62 (4H, br), 3.90 (2H, br), 6.32 (1H, d, J=7Hz), 6.56-6.61 (2H, m), 6.83 (1H, d, J=7Hz), 6.90 (1H, d, J=7Hz), 7.17 (1H, s)

17) 4-Amino-3-hydroxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.62 (6H, br), 2.28 (3H, s), 2.31 (3H, s), 2.38-2.49 (6H, m), 3.28 (3H, s), 3.52 (2H, br), 3.67 (2H, br), 3.78 (2H, br), 3.91 (2H, br), 6.32-6.38 (1H, m), 6.57-6.67 (3H, m), 7.00-7.03 (2H, m)

Preparation 6

[0281] The following compounds were obtained by reacting the compounds, which were prepared according to a similar manner to that of Preparation 4, with hydrogen chloride.

1) Benzyl 4-amino-3-benzyloxybenzoate hydrochloride
NMR (DMSO-d_6, δ) : 5.18 (2H, s), 5.25 (2H, s), 5.98 (2H, br), 6.78 (1H, d, J=7Hz), 7.29-7.52 (12H, m)

2) Methyl 2-amino-5-thiophenecarboxylate hydrochloride
NMR (DMSO-d_6, δ) : 3.68 (3H, s), 5.90 (1H, d, J=5Hz), 7.32-7.37 (2H, m)

Preparation 7

[0282] The following compounds were obtained according to a similar manner to that of Preparation 1.

1) 2-(3-Hydroxyprop-1-yl)oxynitrobenzene
NMR ($CDCl_3$, δ) : 2.07-2.14 (2H, m), 2.22 (1H, t, J=7.5Hz), 3.90 (2H, dd, J=7.5, 7.5Hz), 4.29 (2H, t, J=7Hz), 7.01 (1H, t, J=7Hz), 7.12 (1H, t, J=7Hz), 7.54 (1H, t, J=7Hz), 7.89 (1H, d, J=7Hz)

2) 3- (3-Ethoxycarbonylprop-1-yl)oxy-4-nitrotoluene
NMR ($CDCl_3$, δ) : 1.24 (3H, t, J=7.5Hz), 2.09-2.19 (2H, m), 2.56 (2H, t, J=7.5Hz), 4.08-4.20 (4H, m), 6.81 (1H, d, J=7Hz), 6.97 (1H, s), 7.77 (7H, d)

3) Benzyl 2-(3-phthalimidopropoxy)benzoate
NMR ($CDCl_3$, δ) : 2.08-2.23 (2H, m), 3.85 (2H, t, J=7Hz), 4.07 (2H, t, J=7Hz), 5.32 (2H, s), 6.86-7.02 (2H, m), 7.20-7.50 (6H, m), 7.61-7.74 (2H, m), 7.75-7.90 (3H, m)

4) 2-(5-Ethoxycarbonylpent-1-yloxy)-4-methylnitrobenzene
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7Hz), 1.46-1.63 (2H, m), 1.63-1.78 (2H, m), 1.79-1.94 (2H, m), 2.34 (2H, t, J=7Hz), 2.40 (3H, s), 4.00-4.19 (4H, m), 6.80 (1H, d, J=9Hz), 6.84 (1H, s), 7.76 (1H, d, J=9Hz)

5) 2-Benzyloxy-N-tert-butoxycarbonylaniline
NMR ($CDCl_3$, δ) : 1.49 (9H, s), 5.10 (2H, s), 6.88-6.98 (3H, m), 7.09 (1H, s), 7.32-7.43 (5H, m), 8.10 (1H, br)

6) Methyl 4-[N-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]phenyl]-tert-butoxycarbonylamino]methyl-3-methoxybenzoate

NMR ($CDCl_3$, δ) : 1.33 and 1.42 (total 18H, s), 1.92-2.00 (2H, m), 3.26-3.32 (2H, m), 3.70 and 3.77 (total 3H, s), 3.90 (3H, s), 4.03 (2H, br), 4.72 (2H, br), 6.72-6.97 (3H, m), 7.10-7.23 (2H, m), 7.40-7.53 (2H, m), 7.62 (1H, br)

7) 1-Benzyloxy-2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzene
NMR ($CDCl_3$, δ) : 1.40 and 1.47 (9H, s), 1.98-2.06 (2H, m), 3.23-3.47 (2H, m), 4.10 (2H, t, J=6Hz), 5.18 (2H, s), 5.42 (1H, br), 6.82-6.90 (4H, m), 7.28-7.47 (5H, m)

8) Methyl 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxymethyl-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 1.38 (9H, s), 2.02 (2H, br), 3.38 (2H, br), 3.90-3.92 (6H, m), 4.10-4.16 (2H, m), 5.23 (1H, s), 5.25 (1H, s), 5.44 (1H, br), 6.83-6.92 (4H, m), 7.53-7.57 (2H, m), 7.65-7.69 (1H, m)

9) Benzyl 3-benzyloxy-4-nitrobenzoate
NMR ($CDCl_3$, δ) : 5.28 (2H, s), 5.89 (2H, s), 7.30-7.48 (9H, m), 7.70-7.73 (1H, m), 7.81-7.85 (2H, m)

10) Benzyl 3-benzyloxy-4-[2-[(3-tert-butoxycarbonylamino-prop-1-yl)oxy]benzoyl]aminobenzoate
NMR ($CDCl_3$, δ) : 1.38 (9H, s), 1.60-1.70 (2H, m), 2.95-3.02 (2H, m), 3.80 (2H, t, J=6Hz), 4.42 (1H, br), 5.22 (2H, s), 5.38 (2H, s), 6.93 (1H, d, J=8Hz), 7.10 (1H, t, J=7Hz), 7.32-7.50 (12H, m), 7.71-7.72 (1H, m), 7.80-7.83 (1H, m), 8.23-8.28 (1H, m), 8.78 (1H, d, J=7Hz)

11) Methyl 2-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-5-thiophenecarboxylate

[0283] This compound was used for further reaction without purification.

Preparation 8

[0284] The following compounds were obtained according to a similar manner to that of Preparation 2.

1) 4-[N-Methyl-2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxybenzoic acid
NMR ($CDCl_3$, δ) : 1.45 (9H, s), 1.97-2.06 (2H, m), 3.33-3.42 (5H, m), 3.87 (3H, s), 3.98-4.07 (2H, m), 5.27-5.35 (1H, br), 6.67-6.76 (2H, m) , 7.03-7.19 (3H, m), 7.44-7.50 (2H, m)
ESI-MASS (m/z) : 459 (M+H)

2) 4-Nitro-N-[2-(4-carboxyphenyl)methoxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 3.40 (3H, s), 4.97 (1H, d, J=14Hz), 5.10 (1H, d, J=14Hz), 6.65 (1H, s), 6.68 (1H, d, J=7Hz), 7.00 (1H, d, J=7Hz), 7.33-7.49 (4H, m), 7.97 (2H, d, J=8Hz), 8.10 (2H, d, J=8Hz)

3) 3-Methoxy-4-nitro-N-[2-(4-carboxy)phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.30 (3H, s), 3.42 (3H, s), 3.61 (3H, s), 4.92 (1H, d, J=14Hz), 5.11 (1H, d, J=14Hz), 6.65 (1H, s), 6.73 (1H, d, J=7Hz), 6.86 (1H, d, J=7Hz), 7.02-7.08 (2H, m), 7.48 (2H, d, J=8Hz), 7.54 (1H, d, J=7Hz), 8.16 (2H, d, J=8Hz)

4) 2-(4-Carboxyphenylmethyl)oxy-4-methyl-N,N-dimethylaniline
NMR ($CDCl_3$, δ) : 2.31 (3H, s), 2.89 (6H, s), 5.08 (2H, s), 6.76-7.82 (2H, m), 7.03 (1H, d, J=7Hz), 7.40 (2H, d, J=8Hz), 7.77 (2H, d, J=8Hz)

5) 2-[3-(4-Methoxyphenyl)methoxypropyl-1-yl]thiobenzoic acid
NMR ($CDCl_3$, δ) : 1.95-2.06 (2H, m), 3.03 (2H, t, J=7.5Hz), 3.59 (2H, t, J=7.5Hz), 3.77 (3H, s), 4.46 (2H, s), 6.89 (2H, d, J=8Hz), 7.19 (1H, t, J=7Hz), 7.16 (2H, d, J=8Hz), 7.36 (1H, d, J=7Hz), 7.45 (1H, t, J=7Hz), 8.10 (1H, d, J=7Hz)

6) 4-Amino-3-methoxy-N-[2-(4-carboxy)phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
NMR (DMSO-d_6, δ) : 2.21 (3H, s), 3.15 (3H, s), 3.41 (3H, s), 4.95-5.23 (2H, m), 6.33 (1H, d, J=7Hz), 6.63-6.72 (3H, m), 6.87 (1H, s), 7.04 (1H, d, J=7Hz), 7.44 (2H, d, J=8Hz), 7.95 (2H, d, J=8Hz)

7) 4-Amino-3-methoxy-N-[2-[3-(carboxymethyl)oxyprop-1-yl]oxyphenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.00-2.12 (2H, m), 3.32 (3H, s), 3.60 (3H, s), 3.63-3.74 (2H, m), 3.89-4.14 (2H, m), 4.05 (2H, s), 4.50 (2H, br), 6.40 (1H, d, J=7Hz), 6.80-6.95 (4H, m), 6.95 (1H, d, J=7Hz), 7.16 (1H, t, J=7Hz)

8) 4-Amino-3-methoxy-N-[2-[(E)-5-ethoxycarbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.87-1.99 (2H, m), 2.28 (3H, s), 2.34-2.45 (2H, m), 3.31 (3H, s), 3.61 (3H, s), 3.71-4.00 (2H, m), 5.87 (1H, d, J=15Hz), 6.41 (1H, d, J=7Hz), 6.57-6.68 (2H, m), 6.80-7.12 (4H, m)

9) 3-(5-Carboxypent-1-yloxy)-4-(tert-butoxycarbonylamino)toluene
NMR ($CDCl_3$, δ) : 1.45-1.63 (11H, m), 1.64-1.95 (4H, m), 2.28 (3H, s), 2.42 (2H, t, J=7Hz), 3.99 (2H, t, J=7Hz), 6.65 (1H, s), 6.72 (1H, d, J=8Hz), 6.98 (1H, s), 7.87 (1H, m)

10) 4-[(2-Benzyloxy)benzoyl]amino-3-chlorobenzoic acid
NMR ($CDCl_3$, δ) : 5.49 (2H, s), 7.18 (1H, t, J=6Hz), 7.32-7.42 (4H, m), 7.50-7.62 (3H, m), 7.89-7.93 (2H, m), 8.10 (1H, d, J=7Hz), 8.58-8.62 (1H, m)

11) 4-[2-(Benzyloxy)benzoyl]amino-2-nitrobenzoic acid
NMR (DMSO-d_6, δ) : 5.22 (2H, s), 7.10 (1H, t, J=7Hz), 7.28-7.38 (4H, m), 7.50-7.58 (3H, m), 7.65-7.69 (1H, m), 7.86 (2H, s), 8.16 (1H, s)

12) 2-[2-(Benzyloxy)benzoyl]amino-5-pyridinecarboxylic acid
NMR (DMSO-d_6, δ) : 5.18 (1H, s), 5.32 (2H, s), 6.98-7.20 (2H, m), 7.29-7.67 (6H, m), 7.84-7.88 (1H, m), 8.28-8.37 (2H, m), 8.80 (1H, s)

13) 4-[N-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]phenyl]-tert-butoxycarbonylamino]methyl-3-methoxybenzoic acid
NMR ($CDCl_3$, δ) : 1.35 and 1.43 (total 18H, s), 1.92-2.00 (2H, m), 3.28 and 3.32 (total 2H, m), 3.20 and 3.28 (total 3H, s), 4.02 (2H, br), 4.77 (2H, br), 6.77-7.99 (3H, m), 7.10-7.20 (2H, m), 7.44-7.56 (2H, m), 7.69 (1H, br)

14) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxymethyl-3-methoxybenzoic acid
NMR ($CDCl_3$, δ) : 1.37 (9H, s), 2.05 (2H, br), 3.40 (2H, br), 3.93 (3H, s), 4.10-4.17 (2H, m), 5.27 (2H, s), 5.50 (1H, br), 6.87-6.93 (4H, m), 7.59 (2H, s), 7.72-7.77 (1H, m)

15) 3-Benzyloxy-4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]aminobenzoic acid
NMR (DMSO-d_6, δ) : 1.30 (9H, s), 1.62-1.72 (2H, m), 2.88-2.92 (2H, m), 3.95 (2H, t, J=6Hz), 5.37 (2H, s), 6.80 (1H, br), 7.13 (1H, t, J=7Hz), 7.21 (1H, d, J=7Hz), 7.30-7.67 (9H, m), 8.08 (1H, d, J=7Hz), 8.60 (1H, d, J=7Hz)

16) 2-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-5-thiophenecarboxylic acid
NMR (DMSO-d_6, δ) : 1.32 (9H, s), 1.82-1.90 (2H, m), 3.08-3.14 (2H, m), 4.10 (2H, t, J=6Hz), 6.81 (1H, d, J=5Hz), 6.93-7.00 (1H, m), 7.07 (1H, t, J=7Hz), 7.19 (1H, d, J=7Hz), 7.50-7.58 (2H, m), 7.67 (1H, d, J=7Hz)

Preparation 9

[0285] The following compounds were obtained according to a similar manner to that of Preparation 3.

1) 3-Methoxy-4-nitro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.96 (10H, m), 2.28 (9H, s), 2.30-2.41 (3H, m), 2.58 (1H, m), 3.02 (1H, m), 3.33 (3H, s), 3.77 (3H, s), 3.82-4.00 (3H, m), 4.63 (1H, m), 6.56-6.66 (2H, m), 6.84 (1H, d, J=9Hz), 6.93 (1H, d, J=9Hz), 7.06 (1H, s), 7.61 (1H, d, J=9Hz)

2) 4-Nitro-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.26 (3H, s), 2.32 (3H, s), 2.36-2.57 (4H, m), 3.37 (3H, s), 3.42-3.59 (2H, m), 3.71-3.89 (2H, m), 4.94 (1H, d, J=14Hz), 5.07 (1H, d, J=14Hz), 6.60-6.69 (2H, m), 6.94 (1H, d, J=7Hz), 7.36-7.50 (5H, m), 7.95 (2H, d, J=8Hz)

3) 4-Amino-3-methoxy-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 2.33 (3H, s), 2.37-2.53 (4H, m), 3.36 (3H, s), 3.41-3.54 (2H, m), 3.57 (3H, s), 3.65-3.90 (4H, m), 4.90 (1H, d, J=14Hz), 5.06 (1H, d, J=14Hz), 6.38 (1H, d, J=7Hz), 6.62-6.70 (2H, m), 6.78 (1H, d, J=7Hz), 6.84 (1H, s), 6.98 (1H, d, J=7Hz), 7.33 (2H, d, J=8Hz), 7.41 (2H, d, J=8Hz)

4) 4-Amino-3-methoxy-N-[2-[4-(4-dimethylaminopiperidin-1-yl)carbonyl]phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.14-1.58 (2H, m), 1.75-2.00 (2H, m), 2.26 (3H, s), 2.30 (3H, s), 2.40 (1H, m), 2.73-3.10 (4H, m), 3.36 (3H, s), 3.57 (3H, s), 3.87 (3H, s), 4.83-5.12 (2H, m), 6.39 (1H, d, J=7Hz), 6.61-6.71 (2H, m), 6.28 (1H, d, J=7Hz), 6.33 (1H, s), 6.97 (1H, d, J=7Hz), 7.33 (2H, d, J=8Hz), 7.40 (2H, d, J=8Hz)

5) 4-Amino-3-methoxy-N-methyl-N- [2-[3-(4-methylpiperazin-1-yl)carbonylmethoxyprop-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.98-2.13 (2H, m), 2.27 (3H, s), 2.29-2.38 (4H, m), 3.30 (3H, s), 3.36-3.47 (2H, m), 3.52-3.74 (4H, m), 3.60 (3H, s), 3.94-4.17 (2H, m), 4.11 (2H, s), 6.42 (1H, d, J=7Hz), 6.78-6.92 (4H, m), 7.00 (1H, d, J=7Hz), 7.14 (1H, t, J=7Hz)

6) 4-Amino-3-methoxy-N-[2-[(E)-5-(4-dimethylaminopiperidin-1-yl)carbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.30-1.47 (2H, m), 1.80-1.98 (2H, m), 2.21 (3H, s), 2.26 (6H, s), 2.26-2.43 (2H, m), 2.45-3.67 (6H, m), 3.30 (3H, s), 3.61 (3H, s), 3.85 (2H, br), 3.85-4.04 (2H, m), 4.62 (1H, m), 6.29 (1H, d, J=15Hz), 6.41 (1H, d, J=7Hz), 6.57-6.63 (2H, m), 6.77-6.90 (4H, m)

7) 3-[5-(4-Dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-(tert-butoxycarbonylamino)toluene
NMR ($CDCl_3$, δ) : 1.27-2.00 (19H, m), 2.21-2.44 (12H, m), 2.59 (1H, m), 3.01 (1H, m), 3.89 (1H, m), 4.00 (2H, t, J=7Hz), 4.64 (1H, m), 6.64 (1H, s), 6.72 (1H, d, J=8Hz), 6.94 (1H, s), 7.89 (1H, m)

Preparation 10

[0286] The following compounds were obtained according to a similar manner to that of Example 1.

1) Methyl 4-(2-benzyloxybenzoyl)amino-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 3.50 (3H, s), 3.90 (3H, s), 5.36 (2H, s), 7.08 (1H, d, J=9Hz), 7.15 (1H, t, J=9Hz), 7.33-7.49 (8H, m), 7.73 (1H, dd, J=1, 8Hz), 8.30 (1H, d, J=8Hz), 8.72 (1H, d, J=8Hz)
ESI-MASS (m/z) : 392 (M+H)

2) Methyl 4-(2-acetoxybenzoyl)amino-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 2.38 (3H, s), 3.92 (3H, s), 3.99 (3H, s), 7.19 (1H, d, J=8Hz), 7.38 (1H, t, J=8Hz), 7.55 (1H, t, J=8Hz), 7.60 (1H, s), 7.75 (1H, dd, J=2, 9Hz), 7.99 (1H, dd, J=1, 9Hz), 8.66 (1H, d, J=8Hz), 9.03-9.07 (1H, br s)
ESI-MASS (m/z) : 344 (M+H)

3) 3-Methoxy-4-nitro-N-[2-(4-methoxycarbonyl)-phenylmethoxy-4-methyl]phenylbenzamide
NMR (DMSO-d_6, δ) : 2.31 (3H, s), 3.84 (3H, s), 3.98 (3H, s), 5.27 (2H, s), 6.81 (1H, d, J=7Hz), 7.00 (1H, s), 7.49 (1H, d, J=7Hz), 7.62 (2H, d, J=8Hz), 7.79 (1H, s), 7.92 (2H, d, J=8Hz), 8.00 (1H, d, J=7Hz), 9.85 (1H, s)

4) 4-Nitro-3-methoxy-N-[(E and Z)-2-(4-methoxycarbonylphenyl)ethen-1-yl]phenylbenzamide
NMR ($CDCl_3$, δ) : 3.87 (3Hx2/3, s), 3.91 (3Hx1/3, s), 3.95 (3Hx2/3, s), 4.00 (3Hx1/3, s), 6.71-8.20 (13H, m)

5) 3-Methoxy-4-nitro-N-[2-[3-(ethoxycarbonylmethyl)-oxyprop-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.22 (3H, t, J=7.5Hz), 2.10-2.23 (2H, m), 3.78 (2H, t, J=7.5Hz), 4.01 (2H, s), 4.06 (3H, s), 4.14 (2H, q, J=7.5Hz), 4.26 (2H, t, J=7.5Hz), 6.91-7.06 (3H, m), 7.42 (1H, d, J=7Hz), 7.74 (1H, s), 7.93 (1H, d, J=7Hz), 8.49 (1H, d, J=7Hz), 7.78 (1H, s)

6) 3-Methoxy-4-nitro-N-[2-[(E)-5-ethoxycarbonyl-4-penten-1-yl]oxy-4-methyl]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 1.93-2.08 (2H, m), 2.27-2.50 (2H, m), 2.32 (3H, s), 4.02 (3H, s), 4.01-4.11 (2H, m), 4.18 (2H, q, J=7.5Hz), 5.88 (1H, d, J=15Hz), 6.72 (1H, s), 6.83 (1H, t, J=7Hz), 6.99 (1H, dt, J=15, 7.5Hz), 7.35 (1H, d, J=7Hz), 7.81 (1H, s), 7.92 (1H, d, J=7Hz), 8.28 (1H, d, J=7Hz), 8.45 (1H, s)

7) 4-Benzyloxy-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR (DMSO-d_6, δ) : 1.35-1.49 (2H, m), 1.49-1.63 (2H, m), 1.64-1.79 (2H, m), 2.23 (3H, s), 2.37 (2H, t, J=7Hz), 2.72 (3H, m), 2.78-3.11 (2H, m), 3.16 (3H, s), 3.28-3.60 (5H, m), 3.71-4.13 (5H, m), 4.43 (1H, m), 4.99 (2H, s), 6.63 (1H, d, J=8Hz), 6.80 (2H, d, J=2Hz), 6.86 (2H, s), 6.98 (1H, d, J=8Hz), 7.26-7.44 (5H, m)

8) 3-Methoxy-4-nitro-N-(2-benzyloxy-4-methylphenyl)-benzamide
NMR ($CDCl_3$, δ) : 2.38 (3H, s), 3.90 (3H, s), 5.12 (2H, s), 6.88 (1H, s), 7.30 (1H, s), 7.51 (4H, s), 7.59 (1H, s), 7.82 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz), 8.53 (1H, br)

9) 3-Methyl-4-nitro-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.60 (2H, m), 1.69-1.77 (2H, m), 1.79-1.90 (2H, m), 2.25 (3H, s), 2.29 (3H, s), 2.33-2.42 (6H, m), 2.47 (3H, s), 3.32 (3H, s), 3.45-3.50 (2H, m), 3.58-3.63 (2H, m), 3.82-3.95 (2H, m), 6.55-6.59 (2H, m), 6.83 (1H, d, J=7Hz), 7.14 (1H, d, J=7Hz), 7.37 (1H, s), 7.70 (1H, d, J=7Hz)

10) Ethyl 4-[(2-benzyloxy)benzoyl]amino-3-chlorobenzoate
NMR ($CDCl_3$, δ) : 1.38 (3H, t, J=7Hz), 4.34 (2H, q, J=7Hz), 5.38 (1H, s), 5.39 (1H, s), 7.03-7.16 (2H, m), 7.33-7.50 (6H, m), 7.92-7.99 (2H, m), 8.24-8.32 (1H, m), 8.73-8.29 (1H, m)

11) 3-Hydroxy-4-nitro-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.60 (2H, m), 1.68-1.80 (2H, m), 1.82-1.91 (2H, m), 2.28 (3H, s), 2.30 (3H, s), 2.37-2.42 (6H, m), 3.32 (3H, s), 3.48-3.50 (2H, m), 3.62-3.68 (2H, m), 3.90-3.97 (2H, m), 6.57-6.58 (2H, m), 6.80-6.87 (2H, m), 7.08-7.10 (1H, m), 7.85 (1H, d, J=7Hz)

12) Ethyl 4-[2-(benzyloxy)benzoyl]amino-2-nitrobenzoate
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=7Hz), 4.32 (2H, q, J=7Hz), 5.22-5.30 (2H, m), 7.12-7.27 (2H, m), 7.37-7.69 (9H, m), 8.20-8.34 (1H, m)

13) Methyl 2-[2-(benzyloxy)benzoyl]amino-5-pyridinecarboxylate
NMR ($CDCl_3$, δ) : 3.92 (3H, s), 5.12 (1H, s), 5.36 (2H, s), 6.90-7.01 (1H, m), 7.10-7.18 (2H, m), 7.32-7.55 (5H, m), 8.27-8.34 (2H, m), 8.46 (1H, d, J=6Hz), 8.87-8.88 (1H, m)

14) Benzyl 4-(2-acetoxybenzoyl)amino-3-benzyloxybenzoate
NMR ($CDCl_3$, δ) : 2.05 (3H, s), 5.20 (2H, s), 5.87 (2H, s), 7.13 (1H, d, J=8Hz), 7.32-7.47 (10H, m), 7.50-7.57 (1H, m), 7.73 (1H, s), 7.80 (1H, d, J=8Hz), 7.96 (1H, d, J=8Hz), 8.68 (1H, d, J=7Hz), 9.13 (1H, s)

15) Methyl 2- (2-acetoxybenzoyl)amino-5-thiophenecarboxylate
NMR ($CDCl_3$, δ) : 2.39 (3H, s), 3.88 (3H, s), 6.69 (1H, d, J=5Hz), 7.19-7.21 (1H, m), 7.35-7.30 (iH, m), 7.52-7.59 (1H, m), 7.63-7.66 (1H, m), 7.92-7.95 (1H, m), 9.18 (1H, s)

Preparation 11

[0287] The following compound was obtained by reacting the compound, which was prepared according to a similar manner to that of Example 1, with hydrogen chloride.

4-Benzyloxy-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride

NMR (DMSO-d_6, δ) : 1.35-1.49 (2H, m), 1.49-1.63 (2H, m), 1.64-1.79 (2H, m), 2.23 (3H, s), 2.37 (2H, t, J=7Hz), 2.72 (3H, m), 2.78-3.11 (2H, m), 3.16 (3H, s), 3.28-3.60 (5H, m), 3.71-4.13 (5H, m), 4.43 (1H, m), 4.99 (2H, s), 6.63 (1H, d, J=8Hz), 6.80 (2H, d, J=2Hz), 6.86 (2H, s), 6.98 (1H, d, J=8Hz), 7.26-7.44 (5H, m)

Preparation 12

[0288] The following compound was obtained according to a similar manner to that of Example 4.

4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxybenzoic acid

NMR (DMSO-d_6, δ) : 1.35 (9H, s), 2.04 (2H, quintet, J=7Hz), 3.13 (2H, q, J=7Hz), 3.98 (3H, s), 4.29 (2H, t, J=7Hz), 6.95-7.00 (1H, m), 7.16 (1H, t, J=8Hz), 7.28 (1H, d, J=8Hz), 7.57-7.65 (3H, m), 8.11 (1H, dd, J=1, 8Hz), 8.63 (1H, d, J=8Hz)

ESI-MASS (m/z) : 445 (M+H)

Preparation 13

[0289] The following compounds were obtained according to a similar manner to that of Example 10.

1) 4-Hydroxy-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.44-1.59 (2H, m), 1.62-1.92 (4H, m), 2.22-2.45 (12H, m), 3.31 (3H, 5), 3.42-3.53 (2H, m), 3.58-3.74 (5H, m), 3.77-4.02 (2H, m), 6.53-6.70 (3H, m), 6.80-6.96 (3H, m)

2) Methyl 4-(N-methyl-2-hydroxybenzoylamino)-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 3.37 (3H, s), 3.69 (3H, s), 3.91 (3H, s), 6.38 (1H, t, J=8Hz), 6.72 (1H, d, J=8Hz), 6.91 (1H, d, J=8Hz), 7.15 (1H, t, J=8Hz), 7.21 (1H, d, J=9Hz), 7.49 (1H, d, J=1Hz), 7.62 (1H, dd, J=1, 9Hz)
ESI-MASS (m/z) : 316 (M+H)

3) 4-Hydroxy-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl] benzamide
NMR ($CDCl_3$, δ) : 1.25-2.00 (10H, m), 2.06-2.40 (6H, m), 2.52 (1H, m), 2.73 (6H, br s), 3.02 (1H, m), 3.30 (3H, s), 3.67 (3H, s), 3.76-4.07 (3H, m), 4.82 (1H, m), 6.56-6.72 (3H, m), 6.78-6.96 (3H, m)

4) Methyl 4-[N-(2-hydroxyphenyl)-tert-butoxycarbonylamino]methyl-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 1.38 (9H, s), 3.82 and 3.83 (total 3H, s), 3.90 and 3.91 (total 3H, s), 4.88 (2H, s), 6.80-6.87 (1H, m), 6.95 (1H, br), 7.03-7.12 (2H, m), 7.25-7.30 (2H, m), 7.48-7.50 (1H, m), 7.58-7.60 (1H, m)

5) 2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxyphenol
NMR ($CDCl_3$, δ) : 1.45 (9H, s), 1.95-2.07 (2H, m), 3.25-3.45 (2H, m), 4.10 (2H, t, J=6Hz), 4.68 (1H, br), 6.22 (1H, br), 6.78-6.97 (4H, m)

Preparation 14

[0290] The following compounds were obtained according to a similar manner to that of Example 12.

1) Methyl 4-[N-methyl-2-[(3-tert-butoxycarbonylamino-prop-1-yl)oxy]benzoyl]amino-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 1.43 (9H, s), 1.95-2.05 (2H, m), 3.30-3.40 (5H, m), 3.83 (3H, s), 3.85 (3H, s), 3.96-4.04 (2H, m), 5.23-5.32 (1H, br), 6.65-6.73 (2H, m), 7.00-7.16 (3H, m), 7.38-7.45 (2H, m)
ESI-MASS (m/z) : 473 (M+H)

2) Methyl 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxybenzoate
NMR ($CDCl_3$, 5) : 1.40 (9H, s), 2.13-2.21 (2H, m), 3.33 (2H, q, J=7Hz), 3.92 (3H, s), 4.00 (3H, s), 4.29 (2H, t, J=7Hz), 4.72-4.78 (1H, br), 7.03 (1H, d, J=8Hz), 7.23 (1H, t, J=8Hz), 7.49 (1H, t, J=8Hz), 7.60 (1H, s), 7.75 (1H, d, J=8Hz), 8.27 (1H, d, J=8Hz), 8.77 (1H, d, J=8Hz)
ESI-MASS (m/z) : 459 (M+H)

3) 4-Nitro-N-[2-(4-methoxycarbonylphenyl)methoxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 3.40 (3H, s), 3.94 (3H, s), 4.95 (1H, d, J=14Hz), 5.09 (1H, d, J=14Hz), 6.62 (1H, s), 6.69 (1H, d, J=7Hz), 6.97 (1H, d, J=7Hz), 7.31-7.49 (4H, m), 7.95 (2H, d, J=8Hz), 8.10 (2H, d, J=8Hz)

Preparation 15

[0291] The following compound was obtained according to a similar manner to that of Example 16.
4-Amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.33-1.64 (4H, m), 1.64-1.81 (2H, m), 2.20 (3H, s), 2.29-2.43 (2H, m), 2.73 (3H, s), 2.79-3.10 (4H, m), 3.14 (3H, s), 3.22-3.56 (4H, m), 3.62 (3H, s), 3.72-4.18 (3H, m), 4.42 (1H, m), 6.62 (1H, d, J=8Hz), 6.74-6.92 (3H, m), 6.92-7.10 (2H, m)

Preparation 16

[0292] The following compounds were obtained according to a similar manner to that of Example 43.

1) Methyl 4-(2-hydroxybenzoyl)amino-3-methoxybenzoate
NMR ($CDCl_3$, δ) : 3.93 (3H, s), 4.03 (3H, s), 6.96 (1H, t, J=8Hz), 7.04 (1H, d, J=8Hz), 7.47 (1H, t, J=8Hz), 7.54 (1H, dd, J=1, 8Hz), 7.62 (1H, s), 7.76 (1H, d, J=8Hz), 8.51 (1H, d, J=8Hz), 8.85-8.89 (1H, br s)

ESI-MASS (m/z) : 302 (M+H)

2) Benzyl 3-benzyloxy-4-(2-hydroxybenzoyl)aminobenzoate
NMR ($CDCl_3$, δ) : 5.23 (2H, s), 5.38 (2H, s), 6.82 (1H, t, J=7Hz), 7.01 (1H, d, J=7Hz), 7.30-7.49 (12H, m), 7.70-7.73 (1H, m), 7.80-7.83 (1H, m), 7.52 (1H, d, J=7Hz), 8.95 (1H, s)

3) Methyl 2-(2-hydroxybenzoyl)amino-5-thiophenecarboxylate
NMR (DMSO-d_6, δ) : 3.79 (3H, s), 6.95-7.03 (3H, m), 7.42-7.48 (1H, m), 7.62-7.64 (1H, m), 7.88 (1H, d, J=7Hz)

Preparation 17

[0293] The following compound was obtained according to a similar manner to that of Example 30.
3-Methoxy-4-nitro-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 2.29 (3H, s), 2.35 (3H, s), 2.38-2.54 (4H, m), 3.39 (3H, s), 3.43-3.53 (2H, m), 3.66 (3H, s), 3.71-3.88 (2H, m), 4.92 (1H, d, J=14Hz), 5.07 (1H, d, J=14Hz), 6.65-6.72 (2H, m), 6.87 (1H, d, J=7Hz), 6.98 (1H, d, J=7Hz), 7.03 (1H, s), 7.37 (2H, d, J=8Hz), 7.45 (2H, d, J=8Hz), 7.56 (1H, d, J=7Hz)

Preparation 18

[0294] To a mixture of 2-(4-methoxycarbonylphenyl)methoxy-4-methylaniline (420 mg) and 37% formaldehyde solution (69.7 mg) in a mixture of methanol (10 ml) and acetic acid (0.1 ml) was added sodium cyanoborohydride (146 mg) and the mixture was stirred at ambient temperature for 3 hours. The solution was diluted with ethyl acetate (30 ml) and washed successively with saturated aqueous sodium hydrogen carbonate, water and brine. The organic solution was dried over magnesium sulfate and the solvent was evaporated in vacuo. The residue was purified by silica gel column (chloroform) to give 2-(4-methoxycarbonylphenyl)methoxy-4-methyl-N-methylaniline (356 mg) .
NMR ($CDCl_3$, δ) : 2.22 (3H, s), 2.80 (3H, s), 3.91 (3H, s), 5.11 (2H, s), 6.53 (1H, d, J=7Hz), 6.63 (1H, s), 6.72 (1H, d, J=7Hz), 7.49 (2H, d, J=8Hz), 8.04 (2H, d, J=8Hz)

Preparation 19

[0295] A solution of 2-benzyioxy-N-tert-butoxycarbonylaniline (1 g) in N,N-dimethylformamide (40 ml) was treated with sodium hydride (147 mg, 60% w/w in mineral oil) at 0°C. The reaction mixture was stirred at 0°C for 30 minutes and then at ambient temperature for 1 hour. Methyl 4-bromomethyl-3-methoxybenzoate (909 mg) was added, and the mixture was stirred at ambient temperature for 30 minutes. The reaction was quenched with water and the mixture diluted with ethyl acetate. The organic phase was washed with 0.5K hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine. The solution was concentrated in vacuo and the residue was purified by silica gel column chromatography (hexane:ethyl acetate = 9:1) to give methyl 4-[N-[2-(benzyloxy)phenyl-tert-butoxycarbonylamino]methyl-3-methoxybenzoate (1.38 g).
NMR ($CDCl_3$, δ) : 1.32 and 1.40 (total 9H, s), 3.65 and 3.71 (total 3H, s), 3.90 (3H, s), 4.77 (2H, s), 5.07 (2H, s), 6.78-7.00 (3H, m), 7.09-7.20 (1H, m), 7.27-7.55 (8H, m)

Preparation 20

[0296] The following compounds were obtained according to a similar manner to that of Preparation 19.

1) 4-Nitro-3-methoxy-N-[(E and Z)-2-(4-methoxycarbonylphenyl)ethen-1-yl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.40 (3Hx2/3, s), 3.49 (3Hx1/3, s), 3.54 (3Hx1/3, s), 3.60 (3Hx2/3, s), 3.86 (3Hx2/3, s), 3.95 (3Hx1/3, s), 6.41-8.07 (7H, m)

2) 3-Methoxy-4-nitro-N-[2-[3-(ethoxycarbonylmethyl)-oxyprop-1-yl]oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.04-2.17 (2H, m), 3.37 (3H, s), 3.71 (2H, t, J=7.5Hz), 3.76 (3H, s), 4.06 (3H, s), 4.20 (2H, q, J=7.5Hz), 6.78-7.01 (4H, m), 7.04 (1H, s), 7.19 (1H, t, J=7Hz), 7.60 (1H, d, J=7Hz)

3) 3-Methoxy-4-nitro-N-(2-benzyloxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 3.39 (3H, s), 3.58 (3H, s), 4.85 (1H, d, J=12Hz), 5.07 (1H, d, J=12Hz), 6.68 (2H, s), 6.83 (1H, d, J=9Hz), 6.96 (1H, d, J=9Hz), 7.00 (1H, s), 7.30-7.44 (5H, m), 7.52 (1H, d, J=9Hz)

Preparation 21

[0297] To an ice bath cooled solution of methyl 2-(3-hydroxyprop-1-yl)thiobenzoate (3.7 g) in N,N-dimethylformamide (30 ml) was added sodium hydride (60% in oil, 719 mg) and the solution was stirred at the same temperature for 30 minutes. 4-Methoxybenzyl chloride (2.56 g) was added to the solution and the mixture was stirred at ambient temperature for 5 hours. The mixture was diluted with ethyl acetate (100 ml) and the solution was washed with water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give a crude oil. The crude product was purified by silica gel column chromatography (hexane:ethyl acetate = 10:1) to give methyl 2-[3-(4-methoxyphenyl)methoxyprop-1-yl]thiobenzoate (2.13 g).

NMR ($CDCl_3$, δ) : 1.94-2.07 (2H, m), 3.03 (2H, t, J=7.5Hz), 3.58 (2H, t, J=7.5Hz), 3.80 (3H, s), 3.90 (3H, s), 4.39 (2H, q, J=7.5Hz), 4.45 (2H, s), 6.87 (2H, d, J=8Hz), 7.13 (1H, t, J=7Hz), 7.21-7.46 (4H, m), 7.96 (1H, d, J=7Hz)

Preparation 22

[0298] The following compound was obtained according to a similar manner to that of Preparation 21.

2-[3-(Ethoxycarbonylmethyl)oxyprop-1-yl]oxynitrobenzene

NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7.5Hz), 2.08-2.20 (2H, m), 3.73 (2H, t, J=7.5Hz), 4.06 (2H, s), 4.13-4.32 (4H, m), 7.01 (1H, m), 7.10 (1H, d, J=7Hz), 7.50 (1H, t, J=7Hz), 7.82 (1H, d, J=7Hz)

Preparation 23

[0299] To an ice bath cooled solution of 3-methoxy-4-nitro-N- [2- (4-methoxycarbonyl)phenylmethoxy-4-methyl]-phenylbenzamide (7.67 g) in N,N-dimethylformamide (50 ml) was added sodium hydride (60% in oil, 817 mg) and the solution was stirred at the same temperature for 30 minutes. Iodomethane (1.27 ml) was added to the solution and the mixture was stirred at ambient temperature for 2 hours. The mixture was diluted with ethyl acetate (100 ml) and the solution was washed with water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an oil. The oil was solidified with diethyl ether to give 3-methoxy-4-nitro-N-[2-(4-methoxycarbonyl)phenylmethoxy-4-methyl]phenyl-N-methylbenzamide (6.65 g).

NMR ($CDCl_3$, δ) : 2.28 (3H, s), 3.40 (3H, s), 3.60 (3H, s), 3.94 (3H, s), 4.91 (1H, d, J=14Hz), 5.09 (1H, d, J=14Hz), 6.64 (1H, s), 6.71 (1H, d, J=7Hz), 6.84 (1H, d, J=7Hz), 7.00-7.04 (2H, m), 7.42 (2H, d, J=8Hz), 7.52 (1H, d, J=7Hz), 8.08 (2H, d, J=8Hz)

Preparation 24

[0300] The following compound was obtained according to a similar manner to that of Preparation 23.

3-Methoxy-4-nitro-N-[2-[(E)-5-ethoxycarbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.28 (3H, t, J=7.5Hz), 1.90-2.00 (2H, m), 2.00 (3H, s), 2.34-2.45 (2H, m), 3.35 (3H, s), 3.77 (3H, s), 3.84-3.97 (2H, m), 4.19 (2H, q, J=7.5Hz), 5.88 (1H, d, J=15Hz), 6.58-6.64 (2H, m), 6.84-7.02 (3H, m), 7.07 (1H, s), 7.60 (1H, d, J=7Hz)

Preparation 25

[0301] The following compound was obtained according to a similar manner to that of Example 45.

2-[5-(4-Dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylaniline

NMR ($CDCl_3$, δ) : 1.18-2.00 (10H, m), 2.14-2.69 (13H, m), 2.99 (1H, m), 3.44-4.07 (5H, m), 4.64 (1H, m), 6.45-6.70 (3H, m)

Preparation 26

[0302] The following compound was obtained according to a similar manner to that of Example 38.

2-Hydroxy-N-tert-butoxycarbonylaniline

NMR ($CDCl_3$, δ) : 1.55 (9H, s), 6.63 (1H, s), 6.82-6.89 (1H, m), 6.97-6.99 (1H, m), 7.02-7.08 (2H, m), 8.13 (1H, br)

Preparation 27

[0303] The following compound was obtained according to a similar manner to that of Example 87.

Methyl 2-nitro-5-thiophenecarboxylate

NMR ($CDCl_3$, δ) : 3.95 (3H, s), 7.70 (1H, d, J=5Hz), 7.86-7.88 (1H, m)

Preparation 28

[0304] To a suspension of phosphonium bromide (1.9 g) in tetrahydrofuran (35 ml) at 0°C was added 1.0M lithium bis(trimethylsilyl)amide in tetrahydrofuran (7.88 ml) over 5 minutes period. After 40 minutes, the cooling bath was removed and the red suspension was stirred for 15 minutes at ambient temperature. The suspension was recooled to -78°C, and a solution of 2-[3-(phthalimido)prop-1-yl]oxybenzaldehyde (1.16 g) in 10 ml of tetrahydrofuran (plus a 5 ml rinse) was added via cannula. The red reaction mixture was stirred at 0°C to ambient temperature. After 20 hours, the solution was quenched by 0.5N hydrochloric acid at 0°C. The resulting mixture was concentrated and extracted with chloroform. The organic extract was washed with brine and dried over magnesium sulfate, filtered, and concentrated to give 4-[2-[2-[3-(phthalimido)prop-1-yl]oxy]phenyl]vinyl-3-methoxybenzoic acid (2.4 g) .

NMR (DMSO-d_6, δ) : 1.99-2.22 (2H, m), 3.72-3.94 (5H, m), 3.98-4.17 (2H, m), 6.38-7.88 (11H, m)

Preparation 29

[0305] To a suspension of sodium hydride (60% oil suspension, 88.3 mg) in N,N-dimethylformamide (6 ml) was added a solution of methyl 4-(2-benzyloxybenzoyl)amino-3-methoxybenzoate (600 mg) in N,N-dimethylformamide (4 ml) and the mixture was stirred at 0°C for 1 hour. Methyl iodide (0.14 ml) was added dropwise to the above solution and the mixture was stirred at 0°C for 30 minutes. The reaction temperature was raised to ambient temperature over 30 minutes and the reaction was quenched with 1N hydrochloric acid, and then the resulting solution was extracted with ethyl acetate. Drying, filtering and removal of solvents afforded a crude product. The crude product was purified by column chromatography (eluent; hexane:ethyl acetate = 3:1) to give methyl 4-(N-methyl-2-benzyloxybenzoylamino)-3-methoxybenzoate (650 mg) .

NMR ($CDCl_3$, δ) : 3.35 (3H, s), 3.72 (3H, s), 3.87 (3H, s), 4.93-5.00 (2H, m), 6.65 (1H, d, J=8Hz), 6.76 (1H, t, J=8Hz), 7.00-7.12 (2H, m), 7.18-7.23 (1H, m), 7.30-7.43 (6H, m), 8.02 (1H, s)

ESI-MASS (m/z) : 406 (M+H)

Preparation 30

[0306] To a solution of (S)-1,3-butanediol (1.0 g) and triethylamine (1.12 g) in dichloromethane (30 ml) was added portionwise p-toluenesulfonyl chloride (2.12 g) at 0°C, and then the mixture was stirred at ambient temperature for 3 hours and stand overnight. The resulting solution was diluted with dichloromethane (30 ml) and the organic layer was washed successively with 1N hydrochloric acid, saturated sodium bicarbonate aqueous solution and brine. Drying, filtering and removal of solvents afforded (S)-3-hydroxybutyl p-toluenesulfonate (2.26 g).

NMR ($CDCl_3$, δ) : 1.20 (3H, d, J=8Hz), 1.63-1.77 (1H, m), 1.78-1.93 (1H, m), 2.47 (3H, s), 3.89-4.00 (1H, m), 4.08-4.16 (1H, m), 4.20-4.29 (1H, m), 7.37 (2H, d, J=9Hz), 7.80 (2H, d, J=9Hz)

Preparation 31

[0307] A mixture of (S)-3-hydroxybutyl p-toluenesulfonate (2.25 g) and phthalimide potassium salt (3.41 g) in N,N-dimethylformamide (40 ml) was stirred at 60°C for 3.5 hours. The resulting mixture was diluted with water (50 ml) and the aqueous layer was extracted with ethyl acetate. Drying, filtering and removal of solvents afforded a crude product. The crude product was chromatographed on silica gel (eluent; hexane-ethyl acetate = 2:1) to give (S)-4-(phthalimido-1-yl)-2-butanol (910 mg).

NMR ($CDCl_3$, δ) : 1.22 (3H, d, J=7Hz), 1.64-1.88 (2H, m), 2.73 (1H, d, J=4Hz), 3.68-3.78 (1H, m), 3.82-3.89 (2H, m), 7.70-7.77 (2H, m), 7.83-7.89 (2H, m)

Preparation 32

[0308] To an ice-bath cooled solution of 4-methoxycarbonylphenylmethyl-tri-phenylphosphonium bromide (9.75 g) in N,N-dimethylacetamide (50 ml) was added potassium tert-butoxide (2.23 g). After being stirred in an ice-bath for 30 minutes, 2-nitrobenzaldehyde (3.0 g) was added to the solution and the mixture was stirred at the same temperature for 1 hour. The mixture was diluted with ethyl acetate and the solution was washed with water and brine. The organic solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an oil. The crude oil was subjected to silica gel column (10% ethyl acetate in n-hexane). Trans isomer was eluted first (1.4 g) and next cis and trans mixture (3.7 g).

Methyl 4-[(E)-2-(2-nitrophenyl)ethen-1-yl]benzoate

NMR ($CDCl_3$, δ) : 3.92 (3H, s), 7.10 (1H, d, J=15Hz), 7.41-7.50 (2H, m), 7.55-7.79 (4H, m), 8.00 (1H, d, J=7Hz), 8.07 (2H, d, J=8Hz)

Methyl 4-[E and Z)-2-(2-nitrophenyl)ethen-1-yl]benzoate
NMR ($CDCl_3$, δ) : 3.83 (3Hx2/3 (Z), s), 3.91 (3Hx1/3 (E), s), 6.79 (1Hx2/3, d, J=12Hz), 6.98-8.14 (9H+1/3H, m)

Preparation 33

[0309] To a solution of 3-(3-ethoxycarbonylprop-1-yl)oxy-4-nitrotoluene (2.67 g) in dichlormethane (30 ml) was added diisobutylaluminum hydride (1.5 M solution in toluene, 7 ml) at -78°C and the solution was stirred at the same temperature for 2 hours. The reaction was quenched with addition of small amount of water and a mixture of chloroform (30 ml) and 1N hydrochloric acid (20 ml) was added. The organic phase was separated and washed with water and brine. The organic solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an oil. A mixture of the crude aldehyde and carbethoxymethylene triphenylphosphorane (3.49 g) in tetrahydrofuran (20 ml) was stirred at ambient temperature overnight and the solvent was evaporated in vacuo. The residue was subjected to silica gel column and the column was eluted with 10% ethyl acetate in n-hexane to give 3-[(E)-5-ethoxycarbonyl-4-penten-1-yl]oxy-4-nitrotoluene (2.29 g) .
NMR ($CDCl_3$, δ) : 1.27 (2H, t, J=7.5Hz), 1.93-2.04 (2H, m), 2.37 (3H, s), 2.40-2.50 (2H, m), 4.09 (2H, t, J=7.5Hz), 4.18 (2H, q, J=7.5Hz), 5.89 (1H, d, J=15Hz), 6.80 (1H, d, J=7Hz), 6.82 (1H, s), 7.00 (1H, dt, J=15, 7.5Hz), 7.78 (1H, d, J=7Hz)

Preparation 34

[0310] A 300 ml of hydrogenation bottle was flushed with nitrogen, and 10% palladium on carbon (1.5 g) was added into the bottle. A solution of benzyl 2-(3-phthalimidopropyloxy)benzoate (1.50 g) in methanol (50 ml) and 1,4-dioxane (50 ml) was added to the bottle, along with one drop of acetic acid. The mixture was shaken in a Parr apparatus at 3 atm of hydrogen at 35°C for 8 hours. The catalyst was removed by filtration through a bed of Celite, and washed with 1,4-dioxane (20 ml x 2). The combined solution was concentrated with a rotary evaporator to give crude solid. The crude solid in methanol (57 ml) and 1,4-dioxane (10 ml) was heated and the product was recrystallized on cooling. The crystal was collected by filtration, washed with cold methanol (5 ml) and ari-dried to give 2-(3-phthalimidopropyloxy)-benzoic acid (4.18 g).
mp : 155-157°C
NMR (DMSO-d_6, δ) : 1.98-2.14 (2H, m), 3.79 (2H, t, J=7Hz), 4.08 (2H, t, J=7Hz), 6.99 (1H, dd, J=8, 8Hz), 7.08 (1H, d, J=8Hz), 7.47 (1H, m), 7.62 (1H, d, J=8Hz), 7.77-7.92 (4H, m)

Preparation 35

[0311] A mixture of 4-amino-3-methoxy-N-[2-(4-carboxyphenylmethyl)oxy-4-methylphenyl]-N-methylbenzamide (500 mg), ethanolamine (109 mg), triphenylphosphine (936 mg) and carbon tetrachloride (0.57 ml) in a mixture of pyridine and acetonitrile (1:1, 15 ml) was stirred at ambient temperature for 18 hours. The solvent was evaporated and the residue was purified on silica gel column chromatography (SiO_2 0-10% methanol in chloroform) to give 4-amino-3-methoxy-N-[2-[4-[N-(2-hydroxyethyl)-carbamoyl]phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide (392 mg).
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 3.33 (3H, s), 3.48 (3H, s), 3.60 (2H, q, J=5Hz), 3.78-3.84 (2H, m), 4.97 (2H, br), 6.35 (1H, d, J=8Hz), 6.61 (1H, s), 6.68-6.79 (3H, m), 7.04 (1H, d, J=8Hz), 7.11 (1H, br), 7.20 (2H, d, J=8Hz), 7.76 (2H, d, J=8Hz)

Preparation 36

[0312] To an ice-cooled 4-amino-3-methoxy-N-[2-[4-[N-(2-hydroxyethyl)carbamoyl]phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide (387 mg) was added dropwise thionyl chloride (129 mg), and the mixture was stirred at ambient temperature for 1 hour. The resulting mixture was added aqueous sodium hydrogen carbonate solution (15 ml). The solution was extracted with ethyl acetate (10 ml x 3).
The organic layer was washed with brine and dried over magnesium sulfate. The solvent was removed under reduced pressure to give 4-amino-3-methoxy-N-[2-[4-(2-oxazolin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide (315 mg) .
NMR ($CDCl_3$, δ) : 2.26 (3H, s), 3.35 (3H, s), 3.52 (3H, s), 4.08 (2H, t, J=10Hz), 4.25 (2H, t, J=10Hz), 4.94 (1H, br), 5.07 (1H, br), 6.40 (1H, d, J=8Hz), 6.40-6.88 (4H, m), 7.00 (1H, d, J=8Hz), 7.36 (2H, d, J=8Hz), 7.96 (2H, d, J=8Hz)

Preparation 37

[0313] To a solution of 3-bromopropylamine hydrobromide (5.0 g) and diisopropylethylamine (5.90 g) in dichlorometh-

ane (80 ml) was added portionwise 9-fluorenylmethoxycarbonyl chloride (5.91 g) and the mixture was stirred at ambient temperature for 3 hours and stand overnight. The resulting mixture was diluted with dichloromethane (50 ml) and the organic layer was washed successively with 1N hydrochloric acid and brine. Drying, filtering and removal of solvents afforded a crude product. The crude product was triturated with diethyl ether-hexane (1:5) to give 3-(9-fluorenylmethoxycarbonylamino)propyl bromide (7.82 g) .

NMR ($CDCl_3$, δ) : 2.02-2.12 (2H, m), 3.30-3.45 (4H, m), 4.21 (1H, t, J=8Hz), 4.44 (2H, d, J=8Hz), 4.82-4.90 (1H, br), 7.32 (2H, t, J=8Hz), 7.40 (2H, t, J=8Hz), 7.58 (2H, d, J=8Hz), 7.78 (2H, d, J=8Hz)

ESI-MASS (m/z) : 360 (M+H)

Preparation 38

[0314] To a solution of thiosalicylic acid (500 mg) in ethanol (15 ml) and 2N sodium hydroxide aqueous solution (3.2 ml) was added 3-(9-fluorenylmethoxycarbonylamino)-propyl bromide at ambient temperature and the suspension was stirred for 2 hours. The resulting clear solution was diluted with water (20 ml) and acidified with 1N hydrochloric acid (6.5 ml). White crystals were collected by filtration and the solid was washed with ethanol-water (1:3, 15 ml) and then with n-hexane - diethyl ether (2:1, 15 ml) to give 2-[3-(9-fluorenylmethoxycarbonylamino)-propylthio]benzoic acid (1.07 g).

NMR (DMSO-d_6, δ) : 1.69-1.79 (2H, m), 2.90 (2H, t, J=8Hz), 3.08-3.18 (2H, m), 4.21 (1H, t, J=6Hz), 4.32 (2H, d, J=6Hz), 7.20 (1H, t, J=8Hz), 7.28-7.45 (6H, m), 7.50 (1H, t, J=8Hz), 7.68 (2H, d, J=8Hz), 7.85-7.91 (3H, m)

ESI-MASS (m/z) : 434 (M+H)

Example 1

[0315] To a mixture of 2-benzyloxybenzoic acid (1.17 g) and oxalyl chloride (0.536 ml) in dichioromethane (30 ml) was added 2 drops of N,N-dimethylformamide and the mixture was stirred at ambient temperature for 1 hour. After removing a solvent by evaporation, a solution of residual acid chloride in dichloromethane (5 ml) was added to a mixture of 4-amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide (1.97 g) and triethylamine (1.07 ml) in dichloromethane (5 ml) and the resulting solution was stirred at ambient temperature for 3 hours. The reaction mixture was washed successively with 1N hydrochloric acid, water (20 ml) and brine (20 ml), and dried over magnesium sulfate. The solvent was evaporated to give an oil and the crude product was purified by silica gel column (chloroform) to give 4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-(5-ethoxycarbonylpent-l-yloxy)phenyl]benzamide (2.89 g) as a colorless oil.

NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7.5Hz), 1.41-1.54 (2H, m), 1.63-1.75 (2H, m), 1.75-1.85 (2H, m), 2.32 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.80-3.95 (2H, br), 4.12 (2H, q, J=7.5Hz), 5.18 (2H, s), 6.82-6.90 (2H, m), 6.92-7.00 (3H, m), 7.07-7.19 (5H, m), 7.38-7.52 (6H, m), 8.27 (1H, d, J=7Hz)

Example 2

[0316] The following compounds were obtained according to a similar manner to that of Example 1.

1) 4-(2-Benzyloxybenzoyl)amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylaminoprop-1-yloxy]-phenyl] benzamide
NMR ($CDCl_3$, δ) : 2.00 (2H, m), 2.26 (3H, s), 2.32-2.39 (4H, m), 3.32 (3H, s), 3.34-3.41 (6H, m), 3.81-4.02 (2H, m), 5.20 (2H, s), 6.78-7.26 (9H, m), 7.38-7.53 (7H, m), 8.27 (1H, d, J=7Hz)

2) 3-Methoxy-4-(2-nitrobenzoyl)amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy] phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43-1.60 (2H, m), 1.61-1.90 (4H, m), 2.30 (6H, s), 2.31-2.44 (6H, m), 3.33 (3H, s), 3.44-3.53 (2H, m), 3.57-3.67 (2H, m), 3.71 (3H, s), 3.81-4.03 (2H, m), 6.56-6.69 (2H, m), 6.82-6.99 (2H, m), 7.03 (1H, s), 7.57-7.66 (2H, m), 7.67-7.76 (1H, m), 8.02-8.13 (2H, m), 8.21 (1H, d, J=8Hz)

3) 4-(2-Methoxybenzoyl)amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7Hz), 1.43-1.59 (2H, m), 1.63-1.90 (4H, m), 2.26 (3H, s), 2.34 (2H, t, J=7Hz), 3.32 (3H, s), 3.79-3.99 (2H, m), 4.02 (3H, s), 4.11 (2H, q, J=7Hz), 6.53-6.66 (2H, m), 6.87 (1H, d, J=8Hz), 7.01 (1H, d, J=8Hz), 7.12 (1H, dd, J=8, 8Hz), 7.29-7.40 (2H, m), 7.42-7.56 (3H, m), 8.18-8.28 (1H, m), 9.81 (1H, br s)

4) 4-(2-Benzyloxybenzoyl)amino-3-methoxy-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7Hz), 1.42-1.58 (2H, m), 1.62-1.90 (4H, m), 2.32 (2H, t, J=7Hz), 3.28 (3H, s), 3.33

(3H, s), 3.78-4.03 (2H, m), 4.12 (2H, q, J=7Hz), 5.30 (2H, s), 6.72-7.22 (8H, m), 7.28-7.55 (6H, m), 8.20-8.29 (1H, m), 8.38 (1H, d, J=8Hz)

5) 4-[2-(Acetyloxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-2.01 (10H, m), 2.21-2.46 (15H, m), 1.57 (1H, m), 3.02 (1H, m), 3.32 (3H, s), 3.79 (3H, s), 3.83-4.03 (3H, m), 4.69 (1H, m), 6.54-6.67 (2H, m), 6.80-8.33 (8H, m)

6) 4- [2- (Acetyloxy)benzoyl] amino-3-methoxy-N-methyl-N-[4-methyl-2-(5-ethoxycarbonylpent-1-yloxy)phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.44-1.91 (6H, m), 2.21-2.41 (8H, m), 3.32 (3H, s), 3.80 (3H, s), 3.82-4.03 (2H, m), 6.54-6.67 (2H, m), 6.80-6.95 (2H, m), 7.07 (1H, s), 7.15 (1H, d, J=8Hz), 7.35 (1H, m), 7.51 (1H, m), 7.94 (1H, m), 8.28 (1H, d, J=8Hz), 8.87 (1H, s)

7) 4-(2-Benzyloxybenzoyl)amino-2-chloro-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.47-1.98 (6H, m), 2.36 (2H, t, J=7Hz), 3.34 (3H, s), 3.96 (2H, t, J=7Hz), 4.14 (2H, q, J=7Hz), 5.17 (2H, s), 6.64-6.82 (3H, m), 6.96 (1H, d, J=8Hz), 7.02-7.21 (5H, m), 7.41-7.62 (6H, m), 8.25 (1H, m)

8) 4-(2-Acetoxybenzoyl)amino-3-methoxy-N-methyl-N-(2-methylphenyl)benzamide
NMR ($CDCl_3$, δ) : 2.21 (3H, s), 2.31 (3H, s), 3.38 (3H, s), 3.73 (3H, s), 6.87 (1H, d, J=8Hz), 7.00 (1H, s), 7.03-7.24 (5H, m), 7.29-7.43 (1H, m), 7.51 (1H, dd, J=8, 8Hz), 7.92 (1H, d, J=8Hz), 8.30 (1H, d, J=8Hz), 8.87 (1H, br s)

9) 4-(3-Benzyloxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-1.42 (2H, m), 1.50-1.58 (2H, m), 1.67-1.90 (6H, m), 2.28 (3H, s), 2.29 (6H, s), 2.37 (2H, t, J=8Hz), 2.52-2.62 (1H, m), 2.98-3.07 (1H, m), 3.34 (3H, s), 3.78 (3H, s), 3.85-3.98 (3H, m), 4.59-4.67 (1H, m), 5.12 (2H, s), 6.58 (1H, d, J=8Hz), 6.63 (1H, d, J=8Hz), 6.84 (1H, d, J=8Hz), 6.92 (1H, d, J=8Hz), 7.02 (1H, s), 7.12-7.17 (1H, m), 7.33-7.50 (8H, m), 8.28 (1H, d, J=8Hz), 8.48 (1H, s)
ESI-MASS (m/z) : 721 (M+H)

10) 4-(2-Benzyloxybenzoyl)amino-N-[2-(5-ethoxycarbonyl-pent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7.5Hz), 1.43-1.56 (2H, m), 1.65-1.84 (4H, m), 2.25 (3H, s), 2.32 (2H, t, J=7.5Hz), 3.29 (3H, s), 3.77-3.93 (2H, m), 4.12 (2H, q, J=7.5Hz), 5.19 (2H, s), 6.51 (2H, m), 6.81 (1H, d, J=7Hz), 6.98 (2H, d, J=8Hz), 7.07-7.19 (4H, m), 7.39-7.53 (6H, m), 8.27 (1H, d, J=7Hz)

11) 4-(2-Iodobenzoyl)amino-N-[2-(4-methoxyphenyl)-methoxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.35 (3H, s), 3.82 (3H, s), 4.90-5.05 (2H, m), 6.83 (1H, t, J=7Hz), 6.89-6.96 (3H, m), 7.04 (1H, d, J=7Hz), 7.10-7.19 (2H, m), 7.22-7.32 (4H, m), 7.37-7.48 (3H, m), 7.53 (1H, s), 7.88 (1H, d, J=7Hz)

12) 3-Methoxy-4-[2-(4-methoxyphenylmethyl)oxybenzoyl]-amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.31 (3H, s), 2.35-2.52 (2H, m), 3.24 (3H, s), 3.37 (3H, s), 3.40-3.53 (2H, m), 3.62-3.81 (2H, m), 3.39 (3H, s), 4.89 (1H, d, J=14Hz), 5.06 (1H, d, J=14Hz), 5.21 (2H, s), 6.61-6.70 (2H, m), 6.80-7.18 (7H, m), 7.30-7.45 (7H, m), 8.22 (1H, d, J=7Hz), 8.31 (1H, d, J=7Hz)

13) 4-[2-(E)-(2-Ethoxycarbonylethen-1-yl)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7.5Hz), 1.49-1.60 (2H, m), 1.67-1.77 (2H, m), 1.79-1.90 (2H, m), 2.29 (6H, sx2), 2.33-2.43 (6H, m), 3.33 (3H, s), 3.45-3.53 (2H, m), 3.60-3.67 (2H, m), 3.71 (3H, s), 3.85-4.01 (2H, m), 4.23 (2H, q, J=7.5Hz), 6.40 (1H, d, J=15Hz), 6.58-6.67 (2H, m), 6.86 (1H, d, J=7Hz), 6.92 (1H, d, J=7Hz), 7.02 (1H, s), 7.40-7.52 (2H, m), 7.58 (1H, d, J=7Hz), 7.68 (1H, d, J=7Hz), 8.02-8.15 (2H, m), 8.27 (1H, d, J=7Hz)

14) 4-(2-Dimethylamino-4-methyl)phenoxymethyl-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.20 (3H, t, J=7.5Hz), 1.45-1.58 (2H, m), 1.66-1.77 (2H, m), 1.80-1.95 (2H, m), 2.25 (3H, s), 2.29-2.34 (2H, m), 2.31 (3H, s), 2.80 (6H, s), 4.00-4.16 (4H, m), 5.20 (2H, s), 6.68-6.89 (5H, m), 7.58 (2H, d, J=8Hz), 7.88 (2H, d, J=8Hz), 8.37 (1H, d, J=7Hz), 8.50 (1H, s)

15) 4-(2-Benzyloxy)benzoylamino-3-methoxy-N-[(E and Z)-2-(4-methoxycarbonylphenyl)ethen-1-yl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.06 (3Hx2/3, s), 3.10 (3Hx1/3, s), 3.40 (3Hx2/3, s), 3.43 (3Hx1/3, s), 3.46 (3Hx2/3, s), 3.91 (3Hx1/3, s), 5.20 (2Hx2/3, s), 5.27 (2Hx1/3, s), 6.38-8.37 (22H, m)

16) 3-Methoxy-4-[2-[3-(4-methoxyphenyl)methoxyprop-1-yl]thiobenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.58 (2H, m), 1.61-1.73 (2H, m), 1.68-1.92 (4H, m), 2.25 (3H, s), 2.27 (3H, s), 2.30-2.41 (6H, m), 2.99 (2H, t, J=7.5Hz), 3.30 (3H, s), 3.43-3.52 (4H, m), 3.57-3.66 (2H, m), 3.70 (3H, s), 3.78 (3H, s), 3.82-3.90 (2H, m), 4.38 (2H, s), 6.53-6.65 (2H, m), 6.79-6.93 (3H, m), 7.02 (1H, s), 7.17-7.29 (4H, m), 7.33-7.45 (2H, m), 7.65 (1H, d, J=7Hz), 8.29 (1H, d, J=7Hz), 8.80 (1H, s)

17) 4-(2,4-Dimethoxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.43-1.57 (2H, m), 1.64-1.72 (2H, m), 1.72-1.91 (2H, m), 2.24 (3H, s), 2.27 (3H, s), 2.30-2.40 (6H, m), 3.31 (3H, s), 3.42-3.50 (2H, m), 3.59-3.65 (2H, m), 3.77 (3H, s), 3.80 (3H, s), 3.80-4.02 (2H, m), 3.96 (3H, s), 6.52-6.63 (2H, m), 6.81-7.04 (5H, m), 7.79 (1H, m), 8.38 (1H, d, J=7Hz)

18) 4- [2- (Acetoxy)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.61 (2H, m), 1.64-1.93 (4H, m), 2.22-2.46 (15H, m), 3.33 (3H, s), 3.44-3.53 (2H, m), 3.58-3.68 (2H, m), 3.79 (3H, s), 3.82-4.04 (2H, m), 6.54-6.68 (2H, m), 6.80-6.95 (2H, m), 7.04 (1H, s), 7.14 (1H, d, J=8Hz), 7.35 (1H, m), 7.51 (1H, m), 7.92 (1H, m), 8.29 (1H, br d, J=8Hz), 8.86 (1H, s)

19) 4-(2-Benzyloxy-4-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.61 (2H, m), 1.69-1.91 (4H, m), 2.28 (3H, s), 2.30 (3H, s), 2.32-2.44 (6H, m), 2.38 (3H, s), 3.20 (3H, s), 3.32 (3H, s), 3.50 (2H, t, J=5Hz), 3.64 (2H, t, J=4Hz), 3.85-4.06 (2H, m), 4.89 (2H, s), 6.60-6.68 (2H, m), 6.82-6.95 (4H, m), 7.18 (1H, dd, J=2, 7Hz), 7.27-7.40 (5H, m), 7.98 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

20) 4- (2-Benzyloxy-4-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.86 (6H, m), 2.28 (3H, s), 2.30 (3H, s), 2.36 (3H, s), 2.32-2.48 (6H, m), 3.30 (3H, s), 3.45-3.51 (2H, m), 3.60-3.66 (2H, m), 3.63 (3H, s), 3.79-4.00 (2H, m), 5.24 (2H, d, J=9Hz), 6.56-6.68 (2H, m), 6.80-6.93 (5H, m), 7.31-7.58 (5H, m), 8.11 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

21) 4-(2-Benzyloxy-5-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.99 (8H, m), 2.28 (3H, s), 2.31 (3H, s), 2.31-2.45 (6H, m), 3.25 (3H, s), 3.29 (2H, s), 3.48 (3H, s), 3.48-3.53 (2H, m), 3.60-3.64 (2H, m), 3.82-4.01 (2H, m), 5.27 (2H, s), 6.54-6.63 (2H, m), 6.81-6.95 (4H, m), 7.19-7.47 (7H, m), 8.02 (1H, s), 8.36 (1H, d, J=8Hz)

22) 4-(2-Benzyloxy-4-chlorobenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.86 (6H, m), 2.15-2.31 (2H, m), 2.29 (6H, s), 2.30-2.58 (4H, m), 3.28 (3H, s), 3.49 (2H, t, J=5Hz), 3.60 (3H, s), 3.61 (2H, t, J=5Hz), 3.85-4.00 (2H, m), 5.15 (2H, s), 6.54-6.67 (2H, m), 6.83-7.16 (4H, m), 7.34-7.49 (7H, m), 8.01 (1H, d, J=8Hz), 8.19 (1H, d, J=8Hz)

23) 4-(2-Benzyloxy-4-methoxybenzoyl)amino-3-methoxy-N-methyl-N-[2- [5-(4-methylpiperazin-1-ylcarbonyl) pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.44-1.59 (2H, m), 1.63-1.84 (4H, m), 2.28 (3H, s), 2.30 (3H, s), 2.25-2.40 (6H, m), 3.28 (3H, s), 3.30 (3H, s), 3.48 (2H, t, J=4Hz), 3.62 (2H, t, J=4Hz), 3.89-4.01 (2H, m), 5.26 (2H, s), 6.52-6.67 (4H, m), 6.81-6.92 (4H, m), 7.35-7.48 (5H, m), 8.21 (1H, d, J=9Hz), 8.38 (1H, d, J=8Hz)

24) 4-(2-Acetoxybenzoyl)amino-3-methoxy-N-(2-benzyloxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.29 (3H, s), 3.39 (3H, s), 3.60 (3H, s), 4.88 (1H, d, J=12Hz), 5.02 (1H, d, J=12Hz), 6.68-6.73 (2H, m), 6.82 (1H, d, J=8Hz), 7.02 (1H, s), 7.11-7.20 (2H, m), 7.31-7.42 (5H, m), 7.46-7.53 (1H, m), 7.93 (1H, d, J=8Hz), 8.27 (1H, d, J=8Hz), 8.86 (1H, br)

25) 4-(2-Acetoxybenzoyl)amino-3-methoxy-N-[2-[4-(2-oxazolin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.31 (3H, s), 3.39 (3H, s), 3.63 (3H, s), 4.07 (2H, t, J=10Hz), 4.42 (2H, t, J=10Hz), 4.91 (1H, d, J=12Hz), 5.11 (1H, d, J=12Hz), 6.61 (1H, br), 6.77 (1H, d, J=8Hz), 6.82-7.15 (5H, m), 7.24-7.50 (4H, m), 7.90 (2H, d, J=8Hz), 8.20 (1H, d, J=8Hz)

26) 4-[2-[3-(9-Fluorenylmethyl)oxycarbonylaminoprop-1-yl]thiobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-1.92 (12H, m), 2.29 (9H, s), 2.39 (2H, t, J=5Hz), 2.60 (1H, t, J=10Hz), 2.90-3.12 (3H, m), 3.29 (2H, q, J=5Hz), 3.33 (3H, s), 3.75 (3H, s), 3.82-4.00 (4H, m), 4.38 (2H, t, J=4Hz), 6.55-6.67 (3H, m), 6.83 (1H, d, J=8Hz), 6.92 (1H, d, J=8Hz), 7.02 (1H, s), 7.25-7.46 (6H, m), 7.59 (2H, d, J=7Hz), 7.63 (1H, d, J=8Hz), 7.77 (2H, d, J=8Hz), 8.30 (1H, d, J=8Hz), 8.70 (1H, s)

27) 4-[2-(Acetyloxy)benzoyl]amino-3-methyl-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.53 (2H, br), 1.63-1.89 (4H, m), 2.22 (3H, s), 2.30 (3H, s), 2.36 (3H, s), 2.22-2.50 (10H, m), 3.32-3.38 (3H, m), 3.52-3.57 (2H, m), 3.67 (2H, br), 3.95 (2H, br), 6.61 (2H, s), 6.83-6.93 (2H, m), 7.02-7.20 (2H, m), 7.32-7.58 (2H, m), 7.68 (1H, d, J=7Hz), 7.85 (1H, br)

28) 4-[(2-Benzyloxy)benzoyl]amino-3-[(2-benzyloxy)-benzoyl]oxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.44-1.53 (2H, m), 1.60-1.87 (4H, m), 2.28 (3H, s), 2.29 (3H, s), 2.32-2.38 (7H, m), 3.33 (3H, s), 3.43 (2H, br), 3.60 (2H, br), 3.90 (2H, br), 4.79 (2H, s), 4.93 (2H, s), 6.11-6.20 (3H, m), 6.82-7.43 (18H, m), 7.83-7.88 (1H, m), 8.12-8.15 (1H, m), 8.37-8.42 (1H, m)

29) 4-[4-(Benzyloxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.45 (1H, m), 1.47-1.58 (2H, m), 1.60-1.75 (4H, m), 1.78-1.91 (2H, m), 2.27 (9H, s), 2.30-2.40 (3H, m), 2.50-2.63 (1H, m), 2.95-3.07 (1H, m), 3.30 (3H, s), 3.77 (3H, s), 3.82-3.98 (4H, m), 4.56-4.67 (1H, m), 5.11 (2H, s), 6.56-6.62 (2H, m), 6.80-6.93 (2H, m), 7.00-7.05 (3H, m), 7.34-7.45 (4H, m), 7.78-7.82 (2H, m), 8.22-8.30 (1H, m), 8.46 (1H, s)

30) 4-[4-(Benzyloxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.59 (2H, m), 1.69-1.90 (4H, m), 2.28 (3H, s), 2.30 (3H, s), 2.35-2.42 (6H, m), 3.31 (3H, s), 3.48-3.50 (2H, m), 3.62-3.66 (2H, m), 3.78 (3H, s), 3.82-4.00 (2H, m), 5.13 (2H, s), 6.57-6.60 (2H, m), 6.81-6.92 (2H, m), 7.00-7.02 (3H, m), 7.30-7.43 (5H, m), 7.78-7.82 (2H, m), 8.27 (1H, d, J=7Hz), 8.43 (1H, s)

31) 4-[2-(Benzyloxy)benzoyl]amino-2-nitro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.44 (2H, m), 1.50-1.94 (8H, m), 2.20 (3H, s), 2.27 (6H, s), 2.30-2.43 (3H, m), 2.52-2.63 (1H, m), 2.97-3.10 (1H, m), 3.32 (3H, s), 3.85-3.97 (4H, m), 4.57-4.68 (1H, m), 5.20 (2H, s), 6.41-6.48 (2H, m), 6.52 (1H, s), 6.90-6.93 (1H, m), 7.11-7.20 (3H, m), 7.32 (1H, s), 7.48-7.59 (6H, m), 7.69-7.73 (1H, m), 8.29 (1H, d, J=7Hz)

32) 2-[2-(Benzyloxy)benzoyl]amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-5-pyridinecarboxamide
NMR ($CDCl_3$, δ) : 1.30-1.44 (2H, m), 1.44-1.60 (2H, m), 1.60-1.95 (6H, m), 2.20 and 2.28 (total 9H, s), 2.29-2.41 (3H, m), 2.47-2.64 (1H, m), 2.93-3.09 (1H, m), 3.32 (3H, s), 3.79-3.98 (4H, m), 4.57-4.69 (1H, m), 4.97-5.17 (1H, m), 5.32 (1H, s), 6.39-6.50 (1H, m), 6.60-6.78 (2H, m), 6.85-6.90 (1H, m), 7.00-7.12 (2H, m), 7.27-7.50 (7H, m), 7.56-8.25 (2H, m)

Example 3

[0317] To a mixture of 2-benzyloxybenzoic acid (1.55 g) and oxalyl chloride (1.18 ml) in dichloromethane (30 ml) was added 1 drop of N,N-dimethylformamide and the mixture was stirred at ambient temperature for 1 hour. After removing a solvent by evaporation, a solution of residual acid chloride in dichloromethane (30 ml) was added to a mixture of 4-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]phenyl]benzamide

(3.28 g) and pyridine (1.1 ml) in dichloromethane (50 ml) and the mixture was stirred at ambient temperature for 2.5 hours. The mixture was washed with saturated sodium hydrogen carbonate solution and brine, and dried over sodium sulfate. The solvent was removed by evaporation and purified by silica gel column chromatography (SiO_2; 85 g, 2% methanol in dichloromethane) to give 4-(2-benzyloxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]-4-methylphenyl]benzamide (4.5 g).

NMR ($CDCl_3$, δ) : 1.44-1.59 (2H, m), 1.62-1.90 (4H, m), 2.27 (3H, s), 2.28 (3H, s), 2.30-2.43 (6H, m), 3.30 (3H, s), 3.32 (3H, s), 3.43-3.53 (2H, m), 3.57-3.67 (2H, m), 3.78-4.03 (2H, m), 5.30 (2H, s), 6.52-6.66 (2H, m), 6.78-6.96 (3H, m), 7.04 (1H, d, J=9Hz), 7.10 (1H, dd, J=9, 9Hz), 7.30-7.49 (6H, m), 8.20-8.28 (1H, m), 8.37 (1H, d, J=9Hz)

Example 4

[0318] A solution of 4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide (2.80 g) in a mixture of ethanol (50 ml) and 1N sodium hydroxide solution (10 ml) was stirred at ambient temperature for 4 hours. After removing ethanol by evaporation, the aqueous solution was adjusted to pH 2 with iN hydrochloric acid and the mixture was extracted with chloroform (30 x 2) . The organic phase was washed with water (40 ml) and brine (30 ml), and dried over magnesium sulfate. The solvent was evaporated to give 4-(2-benzyloxybenzoyl)-amino-N-methyl-N-[2-(5-carboxylpent-1-yloxy)phenyl]-benzamide (1.76 g) as a colorless oil.

NMR ($CDCl_3$, δ) : 1.45-1.57 (2H, m), 1.66-1.83 (4H, m), 2.37 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.78-3.96 (2H, br), 5.17 (2H, s), 6.75-6.82 (2H, m), 6.93-7.02 (3H, m), 7.10-7.22 (5H, m), 7.36-7.51 (6H, m), 8.28 (1H, d, J=7Hz)

Example 5

[0319] The following compounds were obtained according to a similar manner to that of Example 4.

1) 4-[2-(Carboxymethoxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.63 (2H, m), 1.73 (2H, m), 1.85 (2H, m), 2.28 (3H, s), 2.35-2.41 (6H, m), 3.36 (3H, s), 3.47 (2H, m), 3.61 (2H, m), 3.91 (2H, m), 4.76 (2H, s), 6.72-6.82 (2H, m), 6.86-7.01 (2H, m), 7.07-7.18 (2H, m), 7.35 (2H, d, J=8.5Hz), 7.47 (1H, t, J=7Hz), 7.72 (2H, d, J=8.5Hz), 8.25 (1H, d, J=7Hz)

2) 4-(2-Aminobenzoyl)amino-N-methyl-N-[2-(5-carboxypent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-1.59 (2H, m), 1.64-1.85 (4H, m), 2.27 (3H, s), 2.38 (2H, t, J=7Hz), 3.32 (3H, s), 3.73-4.00 (2H, m), 6.56-6.76 (4H, m), 6.93 (1H, d, J=9Hz), 7.18-7.48 (6H, m), 7.86 (1H, br s)

3) 4-(2-Methoxybenzoyl)amino-N-methyl-N-[2-(5-carboxypent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.62 (2H, m), 1.65-1.88 (4H, m), 2.26 (3H, s), 2.39 (2H, t, J=7Hz), 3.33 (3H, s), 3.73-4.00 (2H, m), 4.01 (3H, s), 6.54-6.68 (2H, m), 6.91 (1H, br d, J=9Hz), 6.99 (1H, d, J=9Hz), 7.10 (1H, dd, J=9, 9Hz), 7.35 (2H, br d, J=9Hz), 7.41-7.57 (3H, m), 8.17-8.27 (1H, m), 9.84 (1H, br s)

4) 4-(2-Benzyloxybenzoyl)amino-3-methoxy-N-methyl-N-[2-(5-carboxypent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43-1.60 (2H, m), 1.62-1.88 (4H, m), 2.38 (2H, t, J=7Hz), 3.28 (3H, s), 3.34 (3H, s), 3.76-4.02 (2H, m), 5.28 (2H, s), 6.74-6.85 (2H, m), 6.86-6.97 (2H, m), 6.97-7.20 (4H, m), 7.28-7.50 (6H, m), 8.16-8.27 (1H, m), 8.36 (1H, d, J=8Hz)

5) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-(5-carboxypent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.31-1.96 (17H, m), 2.00-2.48 (6H, m), 3.14-3.39 (5H, m), 3.62-4.07 (5H, m), 4.10-4.30 (2H, m), 4.86 (1H, m), 6.52-6.72 (2H, m), 6.81-7.16 (5H, m), 7.37-7.53 (2H, m), 8.11-8.51 (2H, m)

6) 4-(2-Benzyloxybenzoyl)amino-2-chloro-N-methyl-N-[2-(5-carboxypent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.67 (2H, m), 1.68-1.98 (4H, m), 2.42 (2H, t, J=7Hz), 3.34 (3H, s), 3.99 (2H, t, J=7Hz), 5.16 (2H, s), 6.65-6.80 (3H, m), 6.98 (1H, d, J=8Hz), 7.02-7.22 (5H, m), 7.40-7.61 (6H, m), 8.24 (1H, m)

7) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]-benzoyl]amino-3-methoxy-N-methyl-N-[4-(5-carboxypent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.80 (8H, m), 2.18-2.27 (2H, m), 2.32-2.40 (2H, m), 3.25-3.35 (2H, m), 3.48 (3H, s), 3.80 (3H, s), 3.93 (2H, t, J=6Hz), 4.19-4.28 (2H, m), 4.73-4.83 (1H, br), 6.73-6.80 (3H, m), 6.93-7.12 (6H, m), 7.46 (1H, t, J=8Hz), 8.17-8.27 (1H, m)

ESI-MASS (m/z) : 686 (M+Na)

8) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-[2-(5-carboxypent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.31-1.80 (6H, m), 1.95-2.07 (4H, m), 2.22 (3H, s), 2.86 (2H, t, J=7.5Hz), 3.16 (3H, s), 3.70 (1H, m), 3.93 (1H, m), 4.16 (2H, t, J=7.5Hz), 6.65 (1H, d, J=7Hz), 6.78 (1H, s), 7.00-7.10 (2H, m), 7.20 (1H, d, J=7Hz), 7.23 (2H, d, J=8Hz), 7.43-7.62 (4H, m)

9) 4-[2-[3-(tert-Butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-[2-(5-carboxypent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.36-1.50 (2H, m), 1.41 (9H, s), 1.50-1.62 (2H, m), 1.66-1.84 (2H, m), 2.05-2.19 (2H, m), 2.25 (3H, s), 2.36-2.44 (2H, m), 3.23-3.41 (2H, m), 3.31 (3H, s), 3.77-4.00 (2H, m), 4.16-4.29 (2H, m), 4.88 (1H, br), 6.53-6.67 (2H, m), 6.98 (2H, d, J=8Hz), 7.08 (1H, m), 7.30-7.53 (3H, m), 8.11 (1H, m)

10) 4-[(2-Benzyloxy)benzoyl]amino-N-[2-(3-carboxyprop-1-yl)oxy]phenyl-N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.90-2.01 (2H, m), 2.42 (2H, t, J=7.5Hz), 3.20 (3H, s), 3.85-4.02 (2H, m), 5.20 (2H, s), 6.85 (1H, t, J=7Hz), 6.98 (1H, d, J=7Hz), 7.09 (1H, t, J=7Hz), 7.15-7.37 (6H, m), 7.49 (2H, d, J=8Hz), 7.62 (1H, d, J=7Hz)

11) 4-(2-Iodobenzoyl)amino-N-[2-(5-carboxypent-1-yl)oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.45-1.58 (2H, m) , 2.65-2.75 (2H, m), 2.75-2.84 (2H, m), 2.35 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.82-3.98 (2H, m), 6.77-6.86 (2H, m), 7.04 (1H, d, J=7Hz), 7.09-7.21 (2H, m), 7.28-7.48 (5H, m), 7.82-7.90 (2H, m)

12) 4- (2-Dimethylamino-4-methyl)phenoxymethyl-N-[2-(5-carboxypent-1-yl)oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.38-1.52 (2H, m), 1.59-1.69 (2H, m), 1.72-1.85 (2H, m), 2.23 (3H, s), 2.25 (3H, s), 2.30 (2H, t, J=7.5Hz), 2.75 (6H, s), 3.33 (3H, s), 3.11-3.25 (2H, m), 3.88-4.00 (2H, m), 5.02 (2H, s), 6.56-6.67 (3H, m), 6.71 (1H, d, J=7Hz), 6.90-6.99 (2H, m), 7.24 (2H, d, J=8Hz), 7.38 (2H, d, J=8Hz)

13) 3-Methoxy-4-[2-[1-(tert-butoxycarbonyl)piperidin-4-yl]oxybenzoyl]amino-N-[2-(5-carboxypent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40-1.57 (2H, m), 1.45 (9H, s), 1.60-1.94 (6H, m), 2.01-2.22 (2H, m), 2.29 (3H, s), 2.38 (2H, t, J=7.5Hz), 2.97-3.20 (2H, m), 3.33 (3H, s), 3.41 (2H, t, J=7.5Hz), 3.71 (3H, s), 3.78-4.00 (2H, m), 4.67 (1H, m), 6.60-6.65 (2H, m), 6.87-7.12 (5H, m), 7.44 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

14) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)amino-1-methylprop-1-yl)oxybenzoyl]amino-N-[2-(5-carboxypent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.42 (3H, d, J=7.5Hz), 1.43-1.96 (8H, m), 2.25 (3H, s), 2.33-2.42 (2H, m), 3.11-3.33 (2H, m), 3.33 (3H, s), 3.65-3.97 (5H, m), 4.70 (1H, m), 6.53-6.70 (2H, m), 6.79-7.13 (4H, m), 7.44 (1H, t, J=7Hz), 8.23 (1H, m), 8.39 (1H, m)

15) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-(3-carboxypyrid-6-yl)methoxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.05-2.16 (2H, m), 2.27 (3H, s), 3.28 (2H, br), 3.42 (3H, br), 3.58 (3H, br), 3.86-4.00 (2H, m), 4.10-4.25 (2H, m), 4.95 (1H, br), 5.16 (1H, br), 6.62 (3H, br), 6.86-7.18 (4H, m), 7.41 (3H, br), 8.14 (1H, br), 8.33 (1H, br), 9.17 (1H, br)

16) 4- [2- (E)-(2-Carboxyethen-1-yl)benzoylamino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.50-2.00 (6H, m), 2.27-2.52 (10H, m), 2.60-2.81 (2H, m), 3.31 (3H, s), 3.43-3.66 (2H, m), 3.83-4.22 (7H, m), 5.60 (1H, m), 6.57 (1H, m), 6.65-6.76 (4H, m), 7.01-7.12 (2H, m), 7.21 (1H, d, J=7Hz), 7.42-7.60 (3H, m), 7.85 (1H, m)

17) 4-[2-(3-Carboxyprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.57 (2H, m), 1.64-1.75 (2H, m), 1.75-1.87 (2H, m), 2.20 (3H, s), 2.34 (3H, s), 2.35-2.50 (6H, m), 2.61-2.74 (2H, m), 3.30 (3H, s), 3.33-3.46 (2H, m), 3.49-3.69 (4H, m), 3.75 (3H, s), 3.90-4.02 (2H, m), 4.17-4.27 (2H, m), 6.56-6.72 (2H, m), 6.83-6.92 (2H, m), 6.93-7.00 (2H, m), 7.07 (1H, t, J=7Hz), 7.43 (1H, t, J=7Hz), 7.43 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

18) 4-[2-(Carboxymethoxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-

1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.51-1.92 (6H, m), 2.02 (3H, s), 2.30 (3H, s), 2.32 (2H, t, J=5Hz), 2.43-2.68 (4H, m), 3.33 (3H, s), 3.40-3.55 (4H, m), 3.72 (3H, s), 3.75-4.07 (2H, m), 4.73 (2H, s), 6.57-6.68 (2H, m), 6.81-7.10 (6H, m), 7.35-7.45 (1H, m), 8.18 (1H, d, J=7Hz), 8.32 (1H, d, J=8Hz)

Example 6

[0320] A mixture of 4-[2-[3-(phthalimido)prop-1-yl]oxy]-benzoylamino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (470 mg) and hydrazine hydrate (158 mg) in ethanol (5 ml) was stirred at ambient temperature for 6 hours and filtered through a bed of Celite. The filtrate was evaporated and the residue was subjected to silica gel column. The column was eluted with a mixture of chloroform, methanol and aqueous ammonia (10:1:0.1). The object fractions were evaporated to give 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]-amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yloxy]phenyl]benzamide (256 mg) as a colorless amorphous.
NMR ($CDCl_3$, δ) : 1.56 (2H, m), 1.74 (2H, m), 1.87 (2H, m), 2.09 (2H, m), 2.29 (3H, s), 2.34-2.43 (6H, m), 2.97 (2H, t, J=7.5Hz), 3.33 (3H, s), 3.50 (2H, m), 3.65 (2H, m), 3.96 (2H, m), 4.30 (2H, t, J=7.5Hz), 6.73-6.83 (2H, m), 6.95-7.03 (2H, m), 7.77-7.16 (2H, m), 7.34 (2H, d, J=8.5Hz), 7.42-7.50 (3H, m), 8.22 (1H, d, J=7Hz)

Example 7

[0321] The following compounds were obtained according to a similar manner to that of Example 6.

1) 4-[2-(3-Aminoprop-1-yl)oxy]benzoylamino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylaminoprop-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 2.00 (2H, m), 2.10 (2H, m), 2.27 (3H, s), 2.34-2.39 (4H, m), 2.98 (2H, t, J=7.5Hz), 3.35 (3H, s), 3.35-3.61 (6H, m), 3.98 (2H, m), 4.30 (2H, t, J=7.5Hz), 6.80-6.91 (2H, m), 7.02 (2H, d, J=7Hz), 7.07-7.21 (3H, m), 7.33-7.51 (5H, m), 8.22 (1H, d, J=7Hz)

2) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.53 (2H, m), 1.70 (2H, m), 1.84 (2H, m), 2.07 (2H, m), 2.26 (3H, s), 2.28 (3H, s), 2.31-2.40 (6H, m), 2.90 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.49 (2H, m), 3.60 (2H, m), 3.89 (3H, s), 3.82-3.99 (2H, m), 4.28 (2H, t, J=7.5Hz), 6.54-6.64 (2H, m), 6.82-6.94 (2H, m), 7.00-7.11 (3H, m), 7.45 (1H, m), 8.20 (1H, m), 8.39 (1H, m)

3) (R)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.42 and 1.45 (total 3H, s), 1.50-1.89 (8H, m), 2.02-2.12 (1H, m), 2.29 (3H, s), 2.31 (3H, s), 2.33-2.42 (6H, m), 2.84-2.90 (2H, m), 3.33 (3H, s), 3.46-3.52 (2H, m), 3.60-3.67 (2H, m), 3.80 (3H, s), 3.87-4.00 (2H, m), 4.78-4.87 (1H, m), 6.58 (1H, d, J=7Hz), 6.65 (1H, s), 6.82-6.92 (2H, m), 7.03-7.10 (3H, m), 7.45 (1H, t, J=8Hz), 8.21 (1H, dd, J=1, 8Hz), 8.40 (1H, d, J=7Hz)
ESI-MASS (m/z) : 674 (M+H)

4) (R)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43 and 1.45 (total 3H, s), 1.46-1.91 (12H, m), 2.02-2.12 (1H, m), 2.29 (9H, s), 2.30-2.41 (4H, m), 2.52-2.63 (1H, m), 2.87 (2H, t, J=8Hz), 2.97-3.07 (1H, m), 3.35 (3H, s), 3.80 (3H, s), 3.87-3.98 (4H, m), 4.59-4.68 (1H, m), 4.79-4.88 (1H, m), 6.59 (1H, d, J=8Hz), 6.64 (1H, s), 6.83-6.93 (2H, m), 7.05-7.10 (3H, m), 7.45 (1H, t, J=8Hz), 8.23 (1H, d, J=9Hz), 8.42 (1H, d, J=8Hz)
ESI-MASS (m/z) : 702 (M+H)

5) (S)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43 and 1.45 (total 3H, s), 1.46-1.92 (12H, m), 2.02-2.13 (1H, m), 2.28 (9H, s), 2.30-2.40 (4H, m), 2.52-2.63 (1H, m), 2.86 (2H, t, J=8Hz), 2.97-3.07 (1H, m), 3.35 (3H, s), 3.81 (3H, s), 3.87-3.98 (4H, m), 4.60-4.68 (1H, m), 4.79-4.89 (1H, m), 6.59 (1H, d, J=8Hz), 6.54 (1H, s), 6.83-6.93 (2H, m), 7.05-7.10 (3H, m), 7.46 (1H, t, J=8Hz), 8.23 (1H, d, J=9Hz), 8.43 (1H, d, J=8Hz)
ESI-MASS (m/z) : 702 (M+H)

6) 4-[2-[4-Aminobut-1-yl)oxybenzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phe-

nylbenzamide
NMR ($CDCl_3$, δ) : 1.47-1.74 (8H, m), 1.77-1.88 (2H, m), 1.95-2.06 (2H, m), 2.27 (3H, s), 2.31-2.40 (4H, m), 2.78 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.45-3.50 (2H, m), 3.58-3.65 (2H, m), 3.84-3.98 (2H, m), 4.20 (2H, t, J=7.5Hz), 6.72-6.80 (2H, m), 6.93-7.00 (2H, m), 7.04-7.14 (2H, m), 7.30 (2H, d, J=8Hz), 7.40-7.48 (3H, m), 8.19 (1H, d, J=7Hz)

7) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.24 (3H, t, J=7.5Hz), 1.44-1.56 (2H, m), 1.63-1.87 (6H, m), 2.06-2.16 (2H, m), 2.28 (3H, s), 2.33 (2H, t, J=7.5Hz), 2.97 (2H, t, J=7.5Hz), 3.30 (3H, s), 3.82-3.96 (2H, m), 4.11 (2H, q, J=7.5Hz), 4.30 (2H, t, J=7.5Hz), 6.54-6.60 (2H, m), 6.83 (1H, d, J=7Hz), 7.00 (1H, d, J=7Hz), 7.09 (1H, t, J=7Hz), 7.30 (2H, d, J=8Hz), 7.41-7.48 (3H, m), 8.20 (1H, d, J=7Hz)

8) 4- [2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylprop-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.03-2.17 (2H, m), 2.29 (3H, s), 2.33-2.42 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.96 (2H, t, J=7.5Hz), 3.38 (3H, s), 3.46-3.53 (2H, m), 3.59-3.68 (2H, m), 3.92-4.08 (2H, m), 4.28 (2H, t, J=7.5Hz), 6.77-6.83 (2H, m), 6.98-7.18 (4H, m), 7.31 (2H, d, J=8Hz), 7.43-7.50 (3H, m), 8.20 (1H, d, J=7Hz)

9) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.02-2.14 (2H, m), 2.37 (3H, s), 2.30 (3H, s), 2.32-2.51 (4H, m), 2.94 (2H, t, J=7.5Hz), 3.35 (3H, s), 3.41-3.57 (2H, m), 3.67-3.86 (2H, m), 4.30 (2H, t, J=7.5Hz), 4.96 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.63-6.71 (2H, m), 6.95-7.02 (2H, m), 7.11 (1H, t, J=7Hz), 7.31 (2H, d, J=8Hz), 7.36-7.50 (7H, m), 8.22 (1H, d, J=7Hz)

10) 4-[2-(4-Amino-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.42-1.90 (10H, m), 2.28 (3H, s), 2.32-2.41 (6H, m), 3.37 (3H, s), 3.46-3.51 (2H, m), 3.59-3.67 (2H, m), 3.82-4.02 (2H, m), 6.73-6.82 (2H, m), 7.00 (1H, d, J=7Hz), 7.08-7.20 (2H, m), 7.35-7.64 (5H, m), 7.81-7.88 (2H, m)

11) 4-[2-(4-Aminobut-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
MASS (m/z) : 614 (M+1)

12) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.01-2.11 (2H, m), 2.28 (3H, s), 2.31 (3H, s), 2.33-2.51 (4H, m), 2.90 (2H, t, J=7.5Hz), 3.39 (3H, s), 3.40-3.52 (2H, m), 3.61-3.86 (2H, m), 3.67 (3H, s), 4.79 (2H, t, J=7.5Hz), 4.90 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.61-6.70 (2H, m), 7.86 (1H, d, J=7Hz), 6.94-7.10 (4H, m), 7.31-7.46 (5H, m), 8.20 (1H, d, J=7Hz), 8.37 (1H, d, J=7Hz)

13) 3-Methoxy-4-[2-(3-aminoprop-1-yl)oxy]phenylmethyl]-amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.45-1.54 (2H, m), 1.62-1.71 (2H, m), 1.76-1.85 (2H, m), 1.87-2.00 (2H, m), 2.27 (3H, s), 2.30 (3H, s), 2.31-2.40 (4H, m), 2.90 (2H, t, J=7.5Hz), 3.28 (3H, s), 3.45-3.50 (2H, m), 3.57-3.64 (2H, m), 3.61 (3H, s), 3.80-3.97 (2H, m), 4.07 (2H, t, J=7.5Hz), 4.27 (2H, s), 4.70 (1H, br), 6.37 (1H, d, J=7Hz), 6.59 (1H, d, J=7Hz), 6.62 (1H, s), 6.78 (1H, s), 6.82-6.90 (4H, m), 7.16-7.71 (2H, m)

14) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenyleth-1-yl]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.00-2.11 (2H, m), 2.29 (3H, s), 2.32-2.50 (4H, m), 2.61-2.93 (6H, m), 3.32 (3H, s), 3.35-3.89 (2H, m), 3.59-3.81 (2H, m), 3.71 (3H, s), 4.22-4.32 (2H, m), 6.83 (1H, d, J=7Hz), 6.94-7.33 (11H, m), 7.43 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

15) 4-[2-(3-Aminoprop-1-yl)thiobenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
MASS (m/z) : 676 (M+1)

16) 4-[2-(3-Aminoprop-1-yl)sulfonylbenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
MASS (m/z) : 724 (M+1)

17) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(4-dimethylaminopiperidin-1-yl)carbonyl]-phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
MASS (m/z) : 708 (M+1)

18) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonyl-methoxyprop-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.00-2.14 (4H, m), 2.23 (3H, s), 2.29-2.38 (4H, m), 2.88 (2H, t, J=7.5Hz), 3.35 (3H, s), 3.37-3.45 (2H, m), 3.54-3.61 (2H, m), 3.66-3.76 (2H, m), 3.77 (3H, s), 3.94-4.17 (4H, m), 4.30 (2H, t, J=7.5Hz), 6.75-7.18 (8H, m), 7.45 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.42 (1H, d, J=7Hz)

19) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[(E)-5-(4-dimethylaminopiperidin-1-yl)carbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
MASS (m/z) : 686 (M+1)

20) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-[2-(4-aminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.50-1.67 (2H, m), 1.77-1.89 (2H, m), 2.06-2.21 (2H, m), 2.27 (3H, s), 2.80 (2H, t, J=7.5Hz), 3.23-3.36 (2H, m), 3.36 (3H, s), 3.80 (3H, s), 3.84-4.03 (2H, m), 4.26 (2H, t, J=7.5Hz), 6.57-6.68 (2H, m), 6.83-7.15 (5H, m), 7.45 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

21) 4-[2-(3-Amino-1-methylprop-1-yl)oxybenzoyl]amino-3-methoxy-N-(2-benzyloxy-4-methyl)phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.41 (3H, d, J=7.5Hz), 1.70-1.83 (1H, m), 1.96-2.10 (1H, m), 2.26 (3H, s), 2.80-2.89 (2H, m), 3.37 (3H, s), 3.62 (3H, s), 4.82 (1H, m), 4.89 (1H, d, J=14Hz), 5.07 (1H, d, J=14Hz), 6.63-6.72 (2H, m), 7.86 (1H, d, J=7Hz), 6.98 (1H, d, J=7Hz), 7.02-7.11 (3H, m), 7.28-7.49 (6H, m), 8.22 (1H, d, J=7Hz), 8.37 (1H, d, J=7Hz)

22) 4-[2-(4-Aminobut-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.46-2.03 (10H, m), 2.24 (3H, s), 2.28 (3H, s), 2.31-2.40 (6H, m), 2.73 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.44-3.50 (2H, m), 3.59-3.65 (2H, m), 3.77 (3H, s), 3.83-4.00 (2H, m), 4.20 (2H, t, J=7.5Hz), 6.58 (1H, d, J=7Hz), 7.61 (1H, s), 6.85 (1H, d, J=7Hz), 6.90 (1H, d, J=7Hz), 6.87-7.10 (3H, m), 7.45 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

23) 4-[2-(3-Aminoprop-1-yl)oxy-3-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.49-1.91 (6H, m), 1.96-2.07 (2H, m), 2.27 (3H, s), 2.30 (3H, s), 2.35 (3H, s), 2.32-2.40 (6H, m), 2.95 (2H, t, J=5Hz), 3.32 (3H, s), 3.46-3.53 (2H, m), 3.60-3.67 (2H, m), 3.81 (3H, s), 3.85-4.02 (4H, m), 6.56-6.66 (2H, m), 6.82-7.18 (4H, m), 7.33 (1H, d, J=8Hz), 7.80 (1H, d, J=7Hz), 8.36 (1H, d, J=7Hz)

24) 4-[2-(3-Aminoprop-1-yl)oxy-4-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.90 (6H, m), 2.13-2.25 (2H, m), 2.26 (3H, s), 2.28 (3H, s), 2.30-2.58 (6H, m), 2.37 (3H, s), 2.99 (2H, t, J=5Hz), 3.30 (3H, s), 3.49 (3H, s), 3.49 (2H, t, J=5Hz), 3.61 (2H, t, J=5Hz), 3.79 (3H, s), 3.83-3.92 (2H, m), 4.28 (2H, t, J=5Hz), 6.56-6.65 (2H, m), 6.80-6.93 (4H, m), 7.00 (1H, s), 8.02 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

25) 4-[2-(3-Aminoprop-1-yl)oxy-5-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.49-1.90 (6H, m), 1.98-2.20 (4H, m), 2.28 (3H, s), 2.29 (3H, s), 2.31 (3H, s), 2.31-2.42 (4H, m), 2.95 (2H, t, J=5Hz), 3.31 (3H, s), 3.50 (2H, t, J=4Hz), 3.62 (2H, t, J=4Hz), 3.79 (3H, s), 3.80-4.00 (2H, m), 4.25 (2H, t, J=5Hz), 6.57-6.68 (2H, m), 6.82-7.04 (4H, m), 7.24 (1H, d, J=8Hz), 7.95 (1H, s), 8.39 (1H, d, J=8Hz)

26) 4-[2-(3-Aminoprop-1-yl)oxy-4-chlorobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.48-1.60 (2H, m), 1.62-1.90 (2H, m), 2.10 (2H, t, J=6Hz), 2.27 (3H, s), 2.29 (3H, s), 2.30-2.41 (4H, m), 2.93 (2H, t, J=5Hz), 3.31 (3H, s), 3.45-3.53 (2H, m), 3.58-3.66 (2H, m), 3.78 (3H, s), 3.82-4.01 (2H, m), 4.29 (2H, t, J=5Hz), 6.55-6.68 (2H, m), 6.80-6.91 (2H, m), 6.99-7.10 (4H, m), 8.13 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

27) 4-[2-(3-Aminoprop-1-yl)oxy-4-methoxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.89 (6H, m), 2.04-2.15 (2H, m), 2.28 (3H, s), 2.30 (3H, s), 2.31-2.42 (6H, m), 2.93 (2H, t, J=5Hz), 3.31 (3H, s), 3.44-3.52 (2H, m), 3.57-3.65 (2H, m), 3.79 (3H, s), 3.83 (3H, s), 3.83-4.00 (2H, m), 4.26 (2H, t, J=5Hz), 7.50-7.68 (4H, m), 6.82-6.95 (2H, m), 7.03 (3H, s), 8.16 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

Example 8

[0322] A mixture of 4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-(5-carboxypent-1-yloxy)phenyl]benzamide (1.76 g), N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride (714 mg), N-methylpiperazine (311 mg) and 1-hydroxybenzotriazol (504 mg) in N,N-dimethylformamide (20 ml) was stirred at ambient temperature for 2 hours and the mixture was diluted with ethyl acetate (40 ml). The solution was washed successively with saturated aqueous sodium hydrogen carbonate solution (40 ml), water (40 ml) and brine (40 ml), and dried over magnesium sulfate. The solvent was evaporated to give 4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy] phenyl]benzamide (1.98 g) as a colorless oil.
NMR ($CDCl_3$, δ) : 1.46-1.58 (2H, m), 1.64-1.88 (4H, m), 2.30 (3H, s), 2.32-2.41 (6H, m), 3.32 (3H, s), 3.49 (2H, m), 3.62 (2H, m), 3.81-4.00 (2H, br), 5.20 (2H, s), 6.73-6.82 (2H, m), 6.94-7.00 (3H, m), 7.08-7.20 (5H, m), 7.40-7.53 (6H, m), 8.28 (1H, d, J=7Hz)

Example 9

[0323] The following compound was obtained by using 4-[2-(carboxymethoxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide as a starting compound according to a similar manner to that of Example 8.
4-[2-[(4-Methylpiperazin-1-yl)carbonylmethoxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
MASS : 699 (M+1)

Example 10

[0324] A solution of 4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy] phenyl]benzamide (1.90 g) in methanol (30 ml) was hydrogenated under atmospheric presser in the presence of palladium hydroxide (400 mg) for 6 hours and the catalyst was removed by filtration. The filtrate was evaporated to give 4-(2-hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (1.60 g) as a colorless amorphous.
NMR ($CDCl_3$, δ) : 1.51 (2H, m), 1.66 (2H, m), 1.79 (2H, m), 2.30 (2H, m), 2.63 (3H, s), 2.82-2.95 (4H, m), 3.33 (3H, s), 3.72 (2H, m), 3.86 (2H, m), 3.99 (2H, m), 6.78-6.93 (3H, m), 7.05 (2H, m), 7.17 (1H, t, J=7Hz), 7.27 (2H, d, J=8.5Hz), 7.40 (1H, t, J=7Hz), 7.53 (2H, d, J=8.5Hz), 7.91 (1H, m), 9.21 (1H, br)

Example 11

[0325] The following compounds were obtained according to a similar manner to that of Example 10.

1) 4-(2-Hydroxybenzoyl)amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylaminoprop-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 2.00 (2H, m), 2.71 (3H, s), 2.90-3.09 (4H, m), 3.33 (3H, s), 3.50-3.80 (6H, m), 3.97 (2H, m), 6.76-7.03 (5H, m), 7.11-7.22 (2H, m), 7.29-7.44 (3H, m), 7.45-7.54 (2H, m), 7.88 (1H, m)

2) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.62 (2H, m), 1.65-1.90 (4H, m), 2.29 (3H, s), 2.30-2.43 (2H, m), 2.82 (3H, s), 2.88-3.30 (4H, m), 3.31 (3H, s), 3.48 (3H, s), 3.79 (3H, s), 3.77-4.07 (6H, m), 6.58-6.69 (2H, m), 6.84-7.08 (5H, m), 7.43 (1H, dd, J=9, 9Hz), 7.52 (1H, d, J=9Hz), 8.20 (1H, d, J=9Hz), 8.82 (1H, br s)

3) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.47-1.63 (2H, m), 1.64-1.90 (4H, m), 2.38 (2H, t, J=7Hz), 2.78 (3H, s), 2.90-3.31 (4H, m), 3.33 (3H, s), 3.77 (3H, s), 3.80-4.07 (6H, m), 6.77-7.11 (7H, m), 7.12-7.23 (1H, m), 7.37-7.58 (2H, m), 8.21 (1H, d, J=9Hz), 8.79 (1H, s)

4) 2-Chloro-4-[2-(hydroxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.38-1.98 (6H, m), 2.21-2.46 (2H, m), 2.73 (3H, br s), 2.92-3.25 (4H, m), 3.36 (3H, s), 3.70-4.20 (6H, m), 6.67-6.82 (2H, m), 6.82-7.08 (4H, m), 7.08-7.20 (2H, m), 7.21-7.50 (2H, m), 7.70 (1H, br s), 7.92 (1H, br d, J=8Hz), 9.48 (1H, s)

5) 4-(3-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.34-1.58 (4H, m), 1.64-1.97 (6H, m), 2.28 (3H, s), 2.32 (6H, s), 2.33-2.38 (3H, m), 2.51-2.61 (1H, m), 2.97-3.06 (1H, m), 3.34 (3H, s), 3.78-3.81 (3H, br s), 3.85-3.97 (3H, m), 4.60-4.69 (1H, m), 6.58-6.65 (2H, m), 6.84-7.06 (4H, m), 7.38-7.60 (3H, m), 8.17-8.23 (1H, m)
ESI-MASS (m/z) : 631 (M+H)

6) 4-(2-Hydroxybenzoyl)amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7.5Hz), 1.41-1.53 (2H, m), 1.62-1.84 (4H, m), 2.27 (3H, s), 2.32 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.78-3.97 (2H, m), 4.13 (2H, q, J=7.5Hz), 6.56-6.61 (2H, m), 6.84-6.91 (2H, m), 7.02 (1H, d, J=7Hz), 7.28-7.45 (4H, m), 7.62 (1H, d, J=7Hz), 8.47 (1H, s)

7) 4-(2-Hydroxybenzoyl)amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylprop-1-yl]oxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 2.00 (2H, m), 2.71 (3H, s), 2.90-3.09 (4H, m), 3.33 (3H, s), 3.50-3.80 (6H, m), 3.97 (2H, m), 6.76-7.03 (5H, m), 7.11-7.22 (2H, m), 7.29-7.44 (3H, m), 7.45-7.54 (2H, m), 7.88 (1H, m)

8) 4-(2-Hydroxy)benzoylaminc-3-methoxy-N-methyl-N-[2-[4-(4-methylpiperazin-1-yl)carbonyl]phenyleth-1-yl]phenylbenzamide
MASS (m/z) : 607 (M+1)

9) 4-(2-Hydroxy-3-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.90 (6H, m), 2.27 (6H, s), 2.28 (3H, s), 2.33-2.40 (4H, m), 2.70-2.78 (2H, m), 3.30 (3H, s), 3.80 (3H, s), 3.85-4.10 (6H, m), 6.59-6.65 (2H, m), 6.77-6.97 (6H, m), 8.19 (1H, d, J=8Hz), 8.70 (1H, br s)

10) 4- (2-Hydroxy-4-methylbenzoyl) amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.49-1.91 (6H, m), 2.24 (3H, s), 2.29 (3H, s), 2.32 (3H, s), 2.30-2.42 (6H, m), 3.32 (3H, s), 3.49 (2H, t, J=5Hz), 3.63 (2H, t, J=5Hz), 3.80 (3H, s), 3.88-4.01 (2H, m), 6.68-6.65 (2H, m), 6.80 (1H, s), 6.84 (1H, d, J=8Hz), 6.93 (1H, d, J=7Hz), 7.03 (1H, s), 7.37 (1H, d, J=7Hz), 8.19 (1H, d, J=8Hz), 8.71 (1H, br)

11) 4-(2-Hydroxy-4-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.91 (10H, m), 2.28 (3H, s), 2.34 (3H, s), 2.35 (3H, s), 2.30-2.41 (6H, m), 2.80 (2H, br), 3.31 (3H, s), 3.80 (3H, s), 3.81-4.09 (4H, m), 6.60-6.68 (2H, m), 6.84-7.02 (4H, m), 7.20-7.30 (2H, m), 8.20 (1H, br), 8.37 (1H, br)

12) 4-(2-Hydroxy-4-chlorobenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.89 (6H, m), 2.23-2.45 (6H, m), 2.27 (3H, s), 2.32 (3H, s), 3.30 (3H, s), 3.44-3.68 (4H, m), 3.80 (3H, s), 3.80-3.99 (2H, m), 6.53-6.65 (2H, m), 6.72-7.03 (5H, m), 7.41 (1H, d, J=8Hz), 8.12 (1H, d, J=8Hz), 8.74 (1H, br)

13) 4-(2-Hydroxy-4-methoxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.48-1.60 (2H, m), 1.63-1.84 (4H, m), 2.28 (3H, s), 2.37 (2H, t, J=5Hz), 2.25-2.40 (6H, m), 2.79 (3H, s), 3.30 (3H, s), 3.79 (3H, s), 3.82 (3H, s), 3.90-4.01 (2H, m), 6.44-6.50 (2H, m), 6.60-6.66 (2H, m), 6.88-6.97 (3H, m), 7.41 (1H, d, J=8Hz), 8.18 (1H, d, J=8Hz), 8.40 (1H, br)

14) 4- (2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N- [2- [5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.22-1.45 (2H, m), 1.45-1.58 (2H, m), 1.62-1.78 (2H, m), 1.80-1.96 (4H, m), 2.30 (6H, s), 2.30-2.40 (3H, m), 2.50-2.62 (1H, m), 2.97-2.37 (1H, m), 3.37 (3H, s), 3.78 (3H, s), 3.82-4.02 (4H, m), 4.57-4.68 (1H, m), 6.77-7.02 (8H, m), 7.10-7.20 (1H, m), 7.37-7.45 (1H, m), 7.46-7.62 (1H, m), 8.20 (1H, br)

15) 4-(2-Hydroxybenzoyl)amino-3-chloro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-2.08 (10H, m), 2.20-2.60 (13H, m), 2.89-3.05 (1H, m), 3.30 (3H, s), 3.82-4.02 (4H, m), 4.62-4.79 (1H, m), 6.62 (2H, s), 6.73-7.02 (4H, m), 7.28-7.57 (3H, m), 7.99 (1H, d, J=7Hz), 8.42 (1H, d, J=7Hz)

16) 3-Ethoxy-4-(2-hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (3H, t, J=6Hz), 1.47-1.57 (2H, m), 1.65-1.72 (2H, m), 1.78-1.88 (2H, m), 2.27 (3H, s), 2.30 (3H, s), 2.31-2.42 (7H, m), 3.30 (3H, s), 3.48-3.50 (2H, m), 3.52-3.65 (2H, m), 3.82-4.02 (4H, m), 6.58-6.61 (2H, m), 6.82-6.94 (3H, m), 6.98-7.02 (2H, m), 7.40-7.47 (2H, m), 8.20 (1H, d, J=7Hz), 8.83 (1H, s)

17) 3-Hydroxy-4-(2-hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.62 (2H, br), 1.75 (2H, br), 1.85 (2H, br), 2.27 (3H, s), 2.30 (3H, s), 2.42 (7H, br), 3.30 (3H, s), 3.53 (2H, br), 3.68 (3H, br), 3.90 (1H, br), 6.52 (1H, s), 6.63-6.73 (2H, m), 6.87 (1H, t, J=7Hz), 6.97 (1H, d, J=7Hz), 7.08 (1H, d, J=7Hz), 7.15 (1H, s), 7.38 (1H, t, J=7Hz), 7.58 (1H, d, J=7Hz), 7.98 (1H, br), 9.02 (1H, br)

18) 2-(2-Hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-5-pyridinecarboxamide
NMR ($CDCl_3$, δ) : 1.32-2.15 (10H, m), 2.29-2.42 (12H, m), 2.47-2.62 (1H, m), 2.95-3.09 (1H, m), 3.32 (3H, s), 3.75-4.10 (4H, m), 4.58-4.77 (2H, m), 6.33-8.47 (15H, m)

19) 4-(4-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.38-1.55 (4H, m), 1.62-1.72 (2H, m), 1.72-1.83 (2H, m), 1.83-1.97 (2H, m), 2.27 (3H, s), 2.32-2.37 (8H, m), 2.43-2.60 (2H, m), 2.93-3.05 (1H, m), 3.31 (3H, s), 3.70 (3H, s), 3.78-3.95 (4H, m), 4.60-4.70 (1H, m), 6.57-6.60 (2H, m), 6.80-6.97 (5H, m), 7.67 (2H, d, J=7Hz), 8.22 (1H, d, J=7Hz), 8.40 (1H, s)

20) 4-(4-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.58 (2H, m), 1.67-1.75 (2H, m), 1.75-1.87 (2H, m), 2.27 (3H, s), 2.32 (3H, s), 2.38-2.48 (7H, m), 3.35 (3H, s), 3.48-3.53 (2H, m), 3.60-3.70 (2H, m), 3.70 (3H, s), 3.80-3.90 (1H, m), 3.90-4.00 (1H, m), 3.58-3.60 (2H, m), 6.82-6.97 (5H, m), 7.68 (2H, d, J=7Hz), 8.24 (1H, d, J=7Hz), 8.40 (1H, s)

Example 12

[0326] A solution of 4-(2-hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (400 mg) in N,N-dimethylformamide (15 ml) was added potassium carbonate (99 mg) and N-(3-bromopropyl)phthalimide (192 mg) and the mixture was stirred at 60°C for 4 hours. The mixture was poured into water (30 ml) and the aqueous solution was extracted with ethyl acetate (20 ml x 2). The organic phase was washed with water (20 ml) and brine (20 ml), and dried over magnesium sulfate. The solvent was evaporated to give 4-[2-[3-(phthalimido)prop-1-yl]oxy]benzoylamino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (484 mg) as a colorless amorphous.

NMR ($CDCl_3$, δ) : 1.56 (2H, m), 1.63-1.76 (4H, m), 1.86 (2H, m), 2.30 (3H, s), 2.32-2.41 (6H, m), 3.35 (3H, s), 3.50 (2H, m), 3.63 (2H, m), 3.83-3.97 (4H, m), 4.20 (2H, t, J=7.5Hz), 6.73-6.81 (2H, m), 6.92 (1H, d, J=7Hz), 7.00-7.14 (3H, m), 7.32 (2H, d, J=8.5Hz), 7.42 (1H, m), 7.50 (2H, d, J=8.5Hz), 7.65-7.74 (4H, m), 8.08 (1H, d, J=7Hz), 9.69 (1H, s)

Example 13

[0327] The following compounds were obtained according to a similar manner to that of Example 12.

1) 4-[2-(Ethoxycarbonylmethoxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy] phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 1.62 (2H, m), 1.71 (2H, m), 1.83 (2H, m), 2.29 (3H, s), 2.33-2.41 (6H, m), 3.35 (3H, s), 3.49 (2H, m), 3.62 (2H, m), 3.93 (2H, m), 4.33 (2H, q, J=7.5Hz), 4.76 (2H, s), 6.72-6.82 (2H, m), 6.87 (1H, d, J=7Hz), 7.00 (1H, d, J=7Hz), 7.07-7.18 (2H, m), 7.33 (2H, d, J=8.5Hz), 7.46 (1H, t, J=7Hz), 7.71 (2H, d, J=8.5Hz), 8.26 (1H, d, J=7Hz)

2) 4-[2-(3-Piperidinoprop-1-yloxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-l-yloxy] phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45 (2H, m), 1.50-1.60 (4H, m), 1.71 (2H, m), 1.85 (2H, m), 2.14 (2H, m), 2.28 (3H, s), 2.30-2.41 (10H, m), 2.49 (2H, t, J=7.5Hz), 3.34 (3H, s), 3.49 (2H, m), 3.63 (2H, m), 3.94 (2H, m), 4.23 (2H, t, J=7.5Hz), 6.73-6.82 (2H, m), 6.96-7.02 (2H, m), 7.04-7.15 (2H, m), 7.32 (2H, d, J=8.5Hz), 7.43-7.50 (3H, m), 8.22 (1H, d, J=7Hz)

3) 4-[2-[2-(Dimethylamino)eth-1-yloxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.56 (2H, m), 1.70 (2H, m), 1.85 (2H, m), 2.23 (6H, s), 2.30 (3H, s), 2.33-2.41 (6H, m), 2.78 (2H, t, J=7.5Hz), 3.35 (3H, s), 3.50 (2H, m), 3.64 (2H, m), 3.93 (2H, m), 4.22 (2H, t, J=7.5Hz), 6.74-6.81 (2H, m), 6.95-7.01 (2H, m), 7.06-7.15 (2H, m), 7.30 (2H, d, J=8.5Hz), 7.43 (1H, m), 7.56 (2H, d, J=8.5Hz), 8.21 (1H, d, J=7Hz)

4) 4-[2-[3-(Phthalimido)prop-1-yl]oxy]benzoylamino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)-carbonylamino-prop-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 2.01 (2H, m), 2.25 (3H, s), 2.25-2.38 (6H, m), 3.33-3.45 (6H, m), 3.35 (3H, s), 3.87-4.00 (4H, m), 4.21 (2H, t, J=7.5Hz), 6.78-7.00 (3H, m), 7.06-7.20 (3H, m), 7.33-7.56 (4H, m), 7.65-7.75 (4H, m), 7.86 (1H, m), 8.10 (1H, d, J=7Hz), 9.73 (1H, br)

5) 4-[2-[3-(Phthalimido)prop-1-yl]benzoylamino]-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl) pent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.62 (2H, m), 1.63-1.93 (4H, m), 2.10-2.46 (14H, m), 3.33 (3H, s), 3.40-3.53 (2H, m), 3.57-3.68 (2H, m), 3.78 (3H, s), 3.79-4.04 (4H, m), 4.26 (2H, t, J=7Hz), 6.54-6.68 (2H, m), 6.74-7.11 (5H, m), 7.37-7.48 (1H, m), 7.52-7.63 (3H, m), 7.66-7.77 (1H, m), 7.80-7.90 (1H, m), 8.06-8.23 (2H, m)

6) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.63 (2H, m), 1.63-1.93 (6H, m), 2.29 (3H, s), 2.29-2.44 (6H, m), 3.36 (3H, s), 3.44-3.53 (2H, m), 3.58-3.68 (2H, m), 3.76 (3H, s), 3.81-4.05 (4H, m), 4.27 (2H, t, J=7Hz), 6.74-6.91 (3H, m), 6.92-7.20 (5H, m), 7.38-7.48 (1H, m), 7.58 (3H, s), 7.68-7.77 (1H, m), 7.82-7.90 (1H, m), 8.09-8.16 (1H, m), 8.20 (1H, d, J=9Hz)

7) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl) carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-2.00 (12H, m), 2.16-2.48 (12H, m), 2.57 (1H, m), 3.02 (1H, m), 3.33 (3H, s), 3.78 (3H, s), 3.80-4.05 (5H, m), 4.27 (2H, t, J=7Hz), 4.64 (1H, m), 6.56-6.70 (2H, m), 6.78-7.12 (5H, m), 7.43 (1H, m), 7.59 (2H, s), 7.66-7.91 (2H, m), 8.05-8.24 (2H, m)

8) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.34-1.92 (17H, m), 2.23-2.40 (5H, m), 3.20-3.40 (5H, m), 3.78 (3H, s), 3.82-4.01 (2H, m), 4.12 (2H, q, J=7Hz), 4.25 (2H, t, J=7Hz), 4.78 (1H, m), 6.52-6.69 (2H, m), 6.79-7.15 (5H, m), 7.40-7.52 (2H, m), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

9) 2-Chloro-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.51-1.67 (2H, m), 1.68-1.82 (2H, m), 1.82-2.01 (2H, m), 2.22-2.48 (11H, m), 3.38 (3H, s),

3.47-3.56 (2H, m), 3.58-3.69 (2H, m), 3.90 (2H, t, J=7Hz), 3.94-4.11 (2H, m), 4.21 (2H, t, J=7Hz), 6.69-6.82 (2H, m), 6.93 (1H, d, J=8Hz), 7.02-7.20 (4H, m), 7.30 (1H, m), 7.43 (1H, m), 7.68 (4H, s), 8.07 (1H, m), 9.62 (1H, s)

10) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]-benzoyl]amino-3-methoxy-N-methyl-N-(2-methylphenyl)-benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 2.02-2.18 (2H, m), 2.21 (3H, s), 3.21-3.34 (2H, m), 3.39 (3H, s), 3.75 (3H, s), 4.24 (2H, t, J=7Hz), 4.74 (1H, m), 6.83-7.22 (9H, m), 7.44 (1H, m), 8.20 (1H, m), 8.42 (1H, d, J=8Hz)

11) 4-[3-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]-benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-1.45 (2H, m), 1.43 (9H, s), 1.49-1.58 (2H, m), 1.64-1.90 (6H, m), 1.97-2.03 (2H, m), 2.29 (3H, s), 2.30 (6H, s), 2.33-2.39 (3H, m), 2.51-2.61 (1H, m), 2.97-3.07 (1H, m), 3.28-3.38 (2H, m), 3.33 (3H, s), 3.79 (3H, s), 3.86-3.97 (3H, m), 4.08 (2H, t, J=7Hz), 4.59-4.67 (1H, m), 4.70-4.78 (1H, m), 6.57-6.64 (2H, m), 6.84 (1H, d, J=8Hz), 6.93 (1H, d, J=8Hz), 7.02 (1H, s), 7.03-7.07 (1H, m), 7.33-7.40 (3H, m), 8.27 (1H, d, J=8Hz), 8.49 (1H, s)
ESI-MASS (m/z) : 788 (M+1)

12) 4-[2-[4-(Phthalimido)but-1-yl]oxybenzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) :1.48-1.60 (2H, m), 1.65-1.77 (4H, m), 1.80-2.06 (6H, m), 2.29 (3H, s), 2.33-2.41 (6H, m), 3.38 (3H, s), 3.45-3.51 (2H, m), 3.60-3.67 (2H, m), 3.78 (2H, t, J=7.5Hz), 3.88-4.00 (2H, m), 4.23 (2H, d, J=7.5Hz), 6.73-6.42 (2H, m), 6.99 (2H, d, J=8Hz), 7.08-7.17 (2H, m), 7.36 (2H, d, J=8Hz), 7.44-7.50 (3H, m), 7.68-7.77 (2H, m), 7.81-7.91 (2H, m), 8.22 (1H, d, J=7Hz)

13) 4-[2-[3-(Phthalimido)prop-1-yl]oxybenzoyl]amino-N-[2-(5-ethoxycarbonyylpent-1-yl)oxy-4-methyl]phenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.24 (3H, t, J=7.5Hz), 1.45-1.57 (2H, m), 1.64-1.88 (4H, m), 2.25 (3H, s), 2.28-2.37 (4H, m), 3.31 (3H, s), 3.84-3.95 (4H, m), 4.10 (2H, q, J=7.5Hz), 4.20 (2H, t, J=7.5Hz), 6.52-6.62 (2H, m), 6.88 (1H, d, J=7Hz), 6.92 (1H, d, J=7Hz), 7.07 (1H, t, J=7Hz), 7.31 (2H, d, J=8Hz), 7.39-7.50 (3H, m), 7.62-7.64 (4H, m), 8.10 (1H, d, J=7Hz), 9.68 (1H, s)

14) 4-[2-[3-(Phthalimido)prop-1-yl]oxybenzoyl]amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylprop-1-yl]oxy]phenylbenzamide
MASS (m/z) : 718 (M+1)

15) 4-[2-[3-(Phthalimdo)prop-1-yl]oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.25 (3H, s), 2.25-2.31 (2H, m), 2.31 (3H, s), 2.36-2.51 (4H, m), 3.38 (3H, s), 3.63-3.85 (4H, m), 3.91 (2H, t, J=7.5Hz), 4.20 (2H, t, J=7.5Hz), 4.98 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.63-6.70 (2H, m), 6.90-7.00 (2H, m), 7.09 (1H, t, J=7Hz), 7.32 (2H, d, J=8Hz), 7.40-7.77 (7H, m), 8.10 (1H, d, J=7Hz), 9.70 (1H, s)

16) 4-[2-(3-Hydroxyprop-1-yl)oxybenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.43-1.56 (2H, m), 1.60-1.86 (4H, m), 2.11-2.23 (2H, m), 2.14 (3H, s), 2.37-2.90 (6H, m), 3.33 (3H, s), 3.40-3.47 (2H, m), 3.51-3.59 (2H, m), 3.86 (2H, t, J=7.5Hz), 3.86-4.00 (2H, m), 4.32 (2H, t, J=7.5Hz), 6.78-6.85 (2H, m), 6.99-7.19 (4H, m), 7.31 (2H, d, J=8Hz), 7.41-7.53 (3H, m), 8.21 (1H, d, J=8Hz)

17) 4-[2-(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.43-1.54 (2H, m), 1.60-1.70 (2H, m), 1.74-1.85 (2H, m), 2.10-2.21 (2H, m), 2.26 (6H, sx2), 2.30-2.41 (6H, m), 3.32 (3H, s), 3.40-3.48 (2H, m), 3.55-3.61 (2H, m), 3.77 (3H, s), 3.77-4.00 (4H, m), 4.31 (2H, t, J=7.5Hz), 6.57-6.63 (2H, m), 6.85-6.92 (2H, m), 7.00-7.11 (3H, m), 7.44 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

18) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.19-2.32 (2H, m), 2.25 (3H, s), 2.33 (3H, s), 2.36-2.52 (4H, m), 3.33-3.50 (2H, m), 3.39 (3H, s), 3.67 (3H, s), 3.71-3.91 (4H, m), 4.28 (2H, t, J=7.5Hz), 4.95 (1H, d, J=14Hz), 5.09 (1H, d, J=14Hz), 6.62-6.72 (2H,

m), 6.81 (1H, d, J=7Hz), 6.93-7.08 (4H, m), 7.34-7.47 (4H, m), 7.59 (1H, m), 7.68-7.75 (2H, m), 7.82-7.88 (2H, m), 8.10-8.19 (2H, m)

19) 4-[2-(3-Ethoxycarbonylprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxylphenylbenzamide
NMR ($CDCl_3$, δ) : 1.22 (3H, t, J=7.5Hz), 1.45-1.57 (2H, m), 1.63 (3H, s), 1.63-1.73 (2H, m), 1.76-1.88 (2H, m), 2.20-2.32 (2H, m), 2.24 (3H, s), 2.27 (3H, s), 2.32-2.40 (6H, m), 2.50 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.43-3.50 (2H, m), 3.58-3.67 (2H, m), 3.78 (3H, s), 3.83-4.00 (2H, m), 4.12 (2H, q, J=7.5Hz), 4.22 (2H, t, J=7.5Hz), 6.57 (1H, d, J=7Hz), 6.62 (1H, s), 6.80-6.90 (2H, m), 6.97-7.11 (3H, m), 7.45 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

20) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxy]-phenylmethylamino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.57 (2H, m), 1.62-1.72 (2H, m), 1.72-1.95 (4H, m), 2.18 (2H, t, J=7.5Hz), 2.25 (3H, s), 2.28 (3H, s), 2.28-2.43 (4H, m), 3.28 (3H, s), 3.43-3.50 (2H, m), 3.57-3.65 (2H, m), 3.58 (3H, s), 3.80-3.96 (2H, m), 4.02 (2H, t, J=7.5Hz), 4.24 (2H, s), 4.80 (1H, s), 6.27 (1H, d, J=7Hz), 6.60 (1H, d, J=7Hz), 6.64 (1H, s), 6.80-6.95 (5H, m), 7.12-7.21 (2H, m), 7.64-7.88 (4H, m)

21) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2- [4- (4-methylpiperazin-1-yl)carbonyl]phenyleth-1-yl]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.20-2.50 (6H, m), 2.29 (3H, s), 2.61-2.94 (6H, m), 3.30 (3H, s), 3.37-3.68 (2H, m), 3.68 (3H, s), 3.68-3.92 (2H, m), 4.20-4.30 (2H, m), 6.80 (1H, d, J=7Hz), 6.90-6.98 (2H, m), 7.05 (1H, t, J=7Hz), 7.10-7.49 (9H, m), 7.53-7.89 (4H, m), 8.12 (1H, d, J=7Hz), 8.20 (1H, d, J=7Hz)

22) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-[2-[4-(4-dimethylaminopiperidin-1-yl)carbonyl]phenylmethoxy-4-methyl]phenyl-N-methylbenzamide
MASS (m/z) : 824 (M+1)

23) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2- [3-(4-methylpiperazin-1-yl)carbonylmethoxyprop-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.04-2.17 (2H, m), 2.25 (3H, s), 2.28-2.40 (6H, m), 3.33 (3H, s), 3.38-3.46 (2H, m), 3.54-3.62 (2H, m), 3.66-3.76 (2H, m), 3.74 (3H, s), 3.80-3.90 (2H, m), 3.98-4.11 (4H, m), 4.28 (2H, t, J=7.5Hz), 6.78-7.10 (7H, m), 7.14 (1H, t, J=7Hz), 7.43 (1H, t, J=7Hz), 7.55 (2H, s), 7.68-7.75 (1H, m), 7.81-7.90 (1H, m), 8.13 (1H, d, J=7Hz), 8.20 (1H, d, J=7Hz)

24) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-[2-[(E)-5-(4-dimethylaminopiperidin-1-yl)carbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.27-1.47 (2H, m), 1.83-2.02 (2H, m), 2.10-2.48 (6H, m), 2.23 (3H, s), 2.26 (6H, s), 2.50-4.13 (8H, m), 3.32 (3H, s), 3.78 (3H, s), 4.26 (2H, t, J=7.5Hz), 4.62 (2H, m), 6.32 (1H, d, J=15Hz), 6.57-6.67 (2H, m), 6.80-7.16 (5H, m), 7.44 (1H, t, J=7Hz), 7.53-7.88 (5H, m), 7.57 (2H, s), 8.09-8.19 (2H, m)

25) 3-Methoxy-4-[2-(pyrid-3-yl)methoxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.57 (2H, m), 1.63-1.72 (2H, m), 1.75-1.86 (2H, m), 2.27 (3H, s), 2.30 (3H, s), 2.32-2.40 (6H, m), 3.29 (3H, s), 3.31 (3H, s), 3.45-3.51 (2H, m), 3.58-3.65 (2H, m), 3.80-4.00 (2H, m), 5.30 (2H, s), 6.58 (1H, d, J=7Hz), 6.61 (1H, s), 6.83 (1H, d, J=7Hz), 6.88-6.92 (2H, m), 7.05 (1H, d, J=7Hz), 7.14 (1H, t, J=7Hz), 7.29 (1H, m), 7.46 (1H, t, J=7Hz), 7.79 (1H, d, J=7Hz), 8.22 (1H, d, J=7Hz), 8.37 (1H, d, J=7Hz), 8.62 (6H, d, J=7Hz), 8.73 (1H, s)

26) 3-Methoxy-4-[2-[4-(phthalimido)but-1-yl]oxybenzoyl]-amino-N-methyl-N-[4-methyl-2- [5- (4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.46-1.59 (2H, m), 1.65-1.74 (2H, m), 1.78-2.03 (6H, m), 2.26 (3H, s), 2.30 (3H, s), 2.32-2.41 (6H, m), 3.31 (3H, s), 3.43-3.50 (2H, m), 3.60-3.65 (2H, m), 3.74 (2H, t, J=7.5Hz), 3.77 (3H, s), 3.82-4.01 (2H, m), 4.22 (2H, t, J=7.5Hz), 6.58 (1H, d, J=7Hz), 6.63 (1H, s), 6.85 (1H, d, J=7Hz), 6.90 (1H, d, J=7Hz), 7.00 (1H, d, J=7Hz), 7.02 (1H, s), 7.08 (1H, t, J=7Hz), 7.45 (1H, t, J=7Hz), 7.70-7.76 (2H, m), 7.80-7.87 (2H, m), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

27) 4-[2-(3-Dimethylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)car-

bonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.91 (6H, m), 2.07-2.18 (2H, m), 2.25 (6H, s), 2.28 (3H, s), 2.30 (3H, s), 2.32-2.44 (2H, m), 2.48 (2H, t, J=5Hz), 3.32 (3H, s), 3.49 (2H, t, J=5Hz), 3.63 (2H, t, J=3Hz), 3.78 (3H, s), 3.81-3.92 (2H, m), 4.25 (2H, t, J=5Hz), 6.54-6.64 (2H, m), 6.80-6.91 (2H, m), 6.99-7.11 (4H, m), 7.40-7.48 (1H, m) 8.18 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

28) 4-[2-(Ethoxycarbonylmethoxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=5Hz), 1.50-1.91 (6H, m), 2.28 (3H, s), 2.31 (3H, s), 2.35-2.47 (6H, m), 3.33 (3H, s), 3.52 (2H, t, J=5Hz), 3.67 (2H, t, J=5Hz), 3.76 (3H, s), 3.84-4.02 (2H, m), 4.24 (2H, q, J=5Hz), 4.85 (2H, s), 6.55-6.67 (2H, m), 6.81-7.19 (6H, m), 7.41-7.49 (1H, m), 8.20 (1H, d, J=8Hz), 8.34 (1H, d, J=7Hz)

29) 4-[2-[3-(Phthalimido-1-yl)prop-1-yloxy]-3-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.92 (6H, m), 2.14-2.44 (8H, m), 2.25 (3H, s), 2.28 (3H, s), 2.36 (3H, s), 3.33 (3H, s), 3.50 (2H, t, J=5Hz), 3.58 (2H, t, J=5Hz), 3.63 (2H, t, J=5Hz), 3.81 (3H, s), 3.81-4.03 (8H, m), 6.55-6.68 (2H, m), 6.82-7.38 (6H, m), 7.59-7.88 (5H, m), 8.32 (1H, d, J=8Hz)

30) 4-[2-[3-(Phthalimido-1-yl)prop-1-yl]oxy-4-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-1.91 (8H, m), 2.27 (3H, s), 2.30 (3H, s), 2.31-2.42 (6H, m), 2.38 (3H, s), 3.32 (3H, s), 3.50 (2H, t, J=5Hz), 3.63 (2H, t, J=5Hz), 3.78 (3H, s), 3.85-4.02 (6H, m), 4.28 (2H, t, J=5Hz), 6.58-6.67 (2H, m), 6.77 (1H, s), 6.80-6.92 (4H, m), 7.00 (1H, s), 7.58 (4H, s), 8.01 (1H, d, J=8Hz), 8.18 (1H, d, J=8Hz)

31) 4-[2-[3-(Phthalimido-1-yl)propyloxy]-5-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.52-1.91 (10H, m), 2.25 (3H, s), 2.30 (3H, s), 2.31 (3H, s), 2.31-2.45 (2H, m), 3.31 (3H, s), 3.5C (2H, t, J=4Hz), 3.59 (2H, t, J=5Hz), 3.64 (2H, t, J=4Hz), 3.78 (3H, s), 3.85-4.02 (4H, m), 4.24 (2H, t, J=5Hz), 6.58 (2H, m), 6.81-6.92 (3H, m), 7.00 (1H, s), 7.25 (1H, d, J=8Hz), 7.59 (3H, s), 7.71-7.79 (1H, m), 7.82-7.89 (1H, m), 7.92 (1H, s), 8.20 (1H, d, J=8Hz)

32) 4-[2-[3-(Phthalimido-1-yl)propyloxy]-4-chlorobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-1.92 (6H, m), 2.25 (3H, s), 2.30 (3H, s), 2.29-2.44 (8H, m), 3.32 (3H, s), 3.46-3.54 (2H, m), 3.61-3.68 (2H, m), 3.78 (3H, s), 3.80-4.01 (4H, m), 4.25 (2H, t, J=5Hz), 6.56-6.77 (2H, m), 6.79-7.04 (7H, m), 7.44 (2H, s), 7.70-7.78 (1H, m), 7.81-7.88 (1H, m), 8.06 (1H, d, J=8Hz)

33) 4-[2-[3-(Phthalimido-1-yl)propyloxy]-4-methoxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.49-1.90 (6H, m), 2.15-2.24 (2H, m), 2.28 (3H, s), 2.32 (3H, s), 2.30-2.42 (6H, m), 3.33 (3H, s), 3.50 (2H, t, J=4Hz), 3.60 (2H, t, J=5Hz), 3.63 (2H, t, J=4Hz), 3.79 (3H, s), 3.85 (3H, s), 3.82-4.02 (6H, m), 4.24 (2H, t, J=5Hz), 6.57-6.68 (2H, m), 6.82 (1H, d, J=8Hz), 6.89 (1H, d, J=8Hz), 7.00 (1H, s), 7.57 (2H, s), 7.71-7.76 (2H, m), 7.82-7.88 (2H, m), 8.11 (1H, d, J=9Hz), 8.17 (1H, d, J=8Hz)

34) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-(2-benzyloxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.10 (2H, t, J=5Hz), 2.29 (3H, s), 3.28 (2H, q, J=5Hz), 3.39 (3H, s), 3.62 (3H, s), 4.21 (2H, t, J=5Hz), 4.90 (1H, d, J=13Hz), 5.08 (1H, d, J=13Hz), 6.63-6.71 (3H, m), 6.87 (1H, d, J=7Hz), 6.96-7.11 (6H, m), 7.31-7.48 (6H, m), 8.21 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

35) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-[4-(2-oxazolin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.09-2.17 (2H, m), 2.28 (3H, s), 3.27 (1H, q, J=5Hz), 3.40 (3H, s), 3.65 (3H, s), 4.05 (2H, t, J=10Hz), 4.23 (2H, t, J=5Hz), 4.40 (2H, t, J=10Hz), 4.88 (1H, d, J=12Hz), 5.08 (1H, d, J=12Hz), 6.62 (1H, s), 6.68 (1H, d), 6.97-7.11 (6H, m), 7.32 (1H, d, J=8Hz), 7.41 (1H, d, J=8Hz), 7.92 (2H, d, J=8Hz), 8.21 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz)

36) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-

1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.22-1.47 (2H, m), 1.47-1.80 (6H, m), 1.80-1.92 (4H, m), 2.29 (6H, s), 2.31-2.41 (3H, m), 2.50-2.63 (1H, m), 2.95-3.07 (1H, m), 3.36 (3H, s), 3.48 (1H, s), 3.49 (1H, s), 3.75 (3H, s), 3.82-4.03 (4H, m), 4.22-4.30 (2H, m), 4.60-4.70 (1H, m), 6.78-6.90 (3H, m), 6.92-7.20 (4H, m), 7.40-7.50 (1H, m), 7.55-7.63 (3H, m), 7.70-7.80 (1H, m), 7.82-7.90 (1H, m), 8.10-8.22 (2H, m)

37) 3-Methyl-4-[2-[[3-(phthalimido)prop-1-yl]oxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
MASS (m/z) : 774 (M+H)

38) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-chloro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.32-1.45 (2H, m), 1.41 (9H, s), 1.48-1.59 (2H, m), 1.62-1.91 (8H, m), 2.08-2.18 (2H, m), 2.27 (6H, s), 2.28 (3H, s), 2.30-2.40 (3H, m), 2.52-2.61 (1H, m), 2.97-3.07 (1H, m), 3.22-3.30 (2H, m), 3.30 (3H, s), 3.83-4.00 (3H, m), 4.30 (2H, t, J=6Hz), 4.57-4.68 (1H, m), 6.60-6.63 (2H, m), 6.87-6.90 (1H, m), 7.02-7.15 (3H, m), 7.46-7.57 (2H, m), 8.20-8.22 (1H, m), 8.40 (1H, d, J=7Hz)

39) 3-Ethoxy-4-[2-[[3-(phthalimido)prop-1-yl]oxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
MASS (m/z) : 804 (M+H)

40) 3-(3-tert-Butoxycarbonylaminoprop-l-yl)oxy-4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 and 1.43 (total 18H, s), 1.49-1.60 (2H, m), 1.62-1.98 (6H, m), 2.00-2.10 (2H, m), 2.27 (3H, s), 2.29 (3H, s), 2.31-2.41 (6H, m), 3.17-3.29 (4H, m), 3.30 (3H, s), 3.45-3.50 (2H, m), 3.59-3.69 (2H, m), 3.84-4.05 (4H, m), 4.22-4.30 (2H, m), 5.04 (2H, br), 6.55-6.63 (2H, m), 6.85 (1H, d, J=7Hz), 6.93 (1H, d, J=7Hz), 6.98-7.03 (2H, m), 7.09 (1H, t, J=7Hz), 7.43 (1H, t, J=7Hz), 8.14 (1H, d, J=7Hz), 8.36 (1H, d, J=7Hz)

41) 2-Amino-4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-l-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.25-1.39 (2H, m), 1.42 and 1.46 (total 9H, s), 1.48-1.60 (2H, m), 1.62-1.93 (8H, m), 2.08-2.18 (2H, m), 2.27 and 2.28 (total 9H, s), 2.33-2.39 (3H, m), 2.50-2.60 (1H, m), 2.96-3.05 (1H, m), 3.29 (3H, s), 3.31-3.40 (2H, m), 3.85-3.98 (3H, m), 4.19 (2H, t, J=6Hz), 4.57-4.67 (1H, m), 6.57-6.59 (1H, m), 6.63 (2H, s), 6.78-6.89 (2H, m), 6.96 (1H, d, J=7Hz), 7.09 (1H, t, J=6Hz), 7.15 (1H, s), 7.40-7.46 (1H, m), 8.17 (1H, d, J=6Hz)

42) 2-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-5-pyridinecarboxamide
NMR ($CDCl_3$, δ) : 1.30 (9H, s), 1.35-1.93 (12H, m), 2.10-2.22 (2H, m), 2.28 (9H, s), 2.30-2.40 (3H, m), 2.50-2.62 (1H, m), 2.95-3.08 (1H, m), 3.33 (3H, s), 3.38-3.49 (2H, m), 3.82-3.98 (4H, m), 4.29 (2H, t, J=6Hz), 4.57-4.67 (1H, m), 6.60-6.62 (2H, m), 6.90 (1H, d, J=6Hz), 6.99 (1H, d, J=7Hz), 7.09 (1H, t, J=7Hz), 7.44-7.55 (2H, m), 8.13-8.21 (2H, m), 8.39 (1H, s)

Example 14

[0328] To an ice bath cooled solution of 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (200 mg) in dichloromethane (10 ml) were added triethylamine (36.2 mg) and acetic anhydride (36.5 mg) and the mixture was stirred at ambient temperature for 4 hours. The reaction mixture was washed successively with water (10 ml), saturated aqueous sodium hydrogen carbonate solution (10 ml) and brine (10 ml), and dried over magnesium sulfate. The solvent was evaporated to give 4-[2-[(3-acetylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (201 mg) as a colorless amorphous.

NMR ($CDCl_3$, δ) : 1.51 (2H, m), 1.62-1.86 (4H, m), 1.93 (3H, s), 2.11 (2H, m), 2.29 (3H, s), 2.30-2.40 (6H, m), 3.35 (3H, s), 3.40-3.50 (4H, m), 3.59 (2H, m), 3.92 (2H, m), 4.18 (2H, t, J=7.5Hz), 6.28 (1H, m), 6.75-6.83 (2H, m), 6.94-7.17 (4H, m), 7.31 (2H, d, J=8.5Hz), 7.40-7.49 (3H, m), 8.08 (1H, d, J=7Hz), 9.18 (1H, s)

Example 15

[0329] To a mixture of 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbo-

nylpent-1-yloxy]phenyl]benzamide (220 mg) and 37% aqueous formaldehyde (290 mg) in a mixture of methanol (10 ml) and acetic acid (0.2 ml) was added sodium cyanoborohydride (44.8 mg) and the mixture was stirred at ambient temperature for 4 hours. The reaction mixture was diluted with chloroform (20 ml) and the solution was washed successively with saturated aqueous sodium hydrogen carbonate solution (20 ml), water (10 ml) and brine (10 ml). The organic phase was dried over magnesium sulfate and the solvent was evaporated to give 4-[2-[(3-dimethylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (215 mg) as a colorless amorphous.

NMR ($CDCl_3$, δ) : 1.55 (2H, m), 1.73 (2H, m), 1.84 (2H, m), 2.11 (2H, m), 2.20 (6H, s), 2.30 (3H, s), 2.32-2.40 (6H, m), 2.46 (2H, t, J=7.5Hz), 3.35 (3H, s), 3.49 (2H, m), 3.62 (2H, m), 4.24 (2H, t, J=7.5Hz), 6.74-6.83 (2H, m), 6.97-7.03 (2H, m), 7.07-7.16 (2H, m), 7.32 (2H, d, J=8.5Hz), 7.42-7.50 (3H, m), 8.22 (2H, d, J=7Hz)

Example 16

[0330] To a solution of 4-[2-[(3-aminoprop-1-yl)oxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (250 mg) was added 4N hydrogen chloride in ethyl acetate (1 ml) and the solution was stirred at ambient temperature for 10 minutes. The white solid was filtered and dried under reduced pressure to give 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride (205 mg) as a white powder.

NMR (D_2O, δ) : 1.40 (2H, m), 1.59 (2H, m), 1.70 (2H, m), 2.09 (2H, m), 2.42 (2H, t, J=7.5Hz), 2.92 (3H, s), 2.96-3.17 (6H, m), 3.24 (3H, s), 3.41-3.59 (2H, m), 3.69 (1H, m), 3.82 (1H, m), 4.04-4.20 (3H, m), 4.53 (1H, m), 6.72 (1H, d, J=7Hz), 6.81 (1H, t, J=7Hz), 6.93-7.60 (11H, m)

Example 17

[0331] The following compounds were obtained according to a similar manner to that of Example 16.

1) 4-[2-[(3-Acetylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride
NMR (D_2O, δ) : 1.38 (2H, m), 1.50-1.68 (4H, m), 1.48 (2H, m), 1.81 (3H, s), 2.42 (2H, m), 2.90 (3H, s), 2.97-3.15 (6H, m), 3.24 (3H, s), 3.40-3.61 (4H, m), 3.71-3.92 (2H, m), 4.14 (1H, m), 4.54 (1H, m), 6.62-6.77 (2H, m), 6.79-6.90 (2H, m), 7.00 (1H, m), 7.11 (1H, m), 7.19-7.33 (5H, m), 7.59 (1H, d, J=7Hz)

2) 4-[2-[(3-Dimethylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-metylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (D_2O, δ) : 1.51 (2H, m), 1.67 (2H, m), 1.81 (2H, m), 2.22 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.65 (6H, s), 2.82 (3H, s), 3.00-3.17 (2H, m), 3.23 (2H, t, J=7.5Hz), 3.37 (3H, s), 3.89 (1H, m), 4.13 (1H, m), 4.07-4.20 (3H, m), 4.58 (1H, m), 6.92-7.00 (2H, m), 7.11-7.18 (2H, m), 7.26-7.48 (6H, m), 7.54-7.60 (2H, m)

3) 4-[2-[(4-Methylpiperazin-1-yl)carbonylmethoxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (D_2O, δ) : 1.36 (2H, m), 1.53 (2H, m), 1.66 (2H, m), 2.98 (6H, s), 2.91-3.25 (10H, m), 3.30 (3H, s), 3.37-3.69 (4H, m), 3.77-3.96 (2H, m), 4.35-4.56 (2H, m), 4.82 (2H, s), 6.75 (1H, d, J=7Hz), 6.84 (1H, t, J=7Hz), 6.92 (1H, d, J=7Hz), 7.03-7.15 (2H, m), 7.22 (1H, d, J=7Hz), 7.29 (2H, d, J=8.5Hz), 7.43-7.58 (3H, m), 7.80 (1H, d, J=7Hz)

4) 4-[2-(3-Piperidinoprop-1-yloxy)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (D_2O, δ) : 1.42-1.67 (10H, m), 1.78 (2H, m), 2.20 (2H, m), 2.51 (2H, t, J=7.5Hz), 2.65 (2H, m), 2.94 (3H, s), 2.95-3.21 (6H, m), 3.32 (2H, m), 3.35 (3H, s), 3.57 (2H, m), 3.92-4.04 (2H, m), 4.16-4.25 (4H, m), 6.91-6.99 (2H, m), 7.08-7.17 (2H, m), 7.23-7.47 (6H, m), 7.52-7.60 (2H, m)

5) 4-[2-[2-(Dimethylamino)eth-1-yloxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (D_2O, δ) : 1.52 (2H, m), 1.68 (2H, m), 1.81 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.82 (6H, s), 2.93 (3H, s), 2.97-3.21 (4H, m), 3.37 (3H, s), 3.48-3.62 (2H, m), 3.87 (1H, m), 4.01 (1H, m), 4.24 (1H, m), 4.47 (2H, m), 4.57 (1H, m), 6.92-7.00 (2H, m), 7.13-7.48 (8H, m), 7.52-7.62 (2H, m)

6) 4-[2-(3-Aminoprop-1-yl)oxy]benzoylamino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylaminoprop-1-yloxy]phenyl]benzamide dihydrochloride

NMR (D_2O, δ) : 2.01 (2H, m), 2.17 (2H, m), 2.91 (3H, s), 2.95-3.46 (8H, m), 3.40 (3H, s), 3.54 (2H, m), 4.02-4.16 (4H, m), 4.27 (2H, m), 6.93-7.00 (2H, m), 7.12-7.21 (2H, m), 7.26-7.37 (2H, m), 7.39-7.48 (4H, m), 7.54-7.64 (2H, m)

7) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (D_2O, δ) : 1.43 (2H, m), 1.60 (2H, m), 1.72 (2H, m), 2.07 (2H, m), 2.18 (3H, s), 2.45 (2H, t, J=7.5Hz), 2.90 (3H, s), 2.92-3.13 (4H, m), 3.30 (3H, s), 3.41-3.63 (4H, m), 3.64 (3H, s), 3.82 (1H, m), 3.92 (1H, m), 4.04-4.61 (3H, m), 4.50 (1H, m), 6.66-6.74 (3H, m), 6.93-7.04 (3H, m), 7.10 (1H, d, J=7Hz), 7.41 (1H, t, J=7Hz), 7.73 (1H, d, J=7Hz), 7.95 (1H, d, J=7Hz)

8) 4-[2-(3-Aminoprop-1-yl)oxy-4-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.48-1.96 (8H, m), 2.27 (3H, s), 2.32-2.42 (2H, m), 2.78 (3H, s), 3.11-3.22 (2H, m), 3.28 (3H, s), 3.79 (3H, s), 3.80-4.11 (2H, m), 4.22-4.32 (2H, m), 6.58-6.67 (2H, m), 6.79-6.96 (5H, m), 7.87 (1H, d, J=8Hz), 8.69-8.75 (1H, m), 9.41 (1H, br)

9) 4-[2-(3-Aminoprop-1-yl)oxy-3-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.46-1.92 (6H, m), 2.15-2.57 (4H, m), 2.24 (3H, s), 2.30 (3H, s), 2.62-2.98 (6H, m), 2.80 (3H, s), 3.02-3.29 (4H, m), 3.28 (3H, s), 3.73-4.18 (5H, m), 4.46 (1H, br), 4.62 (1H, br), 6.56-6.68 (2H, m), 6.81-6.96 (3H, m), 7.10 (1H, dd, J=2, 8Hz), 7.30 (1H, d, J=8Hz), 7.66-7.77 (1H, m), 8.28-8.52 (4H, m), 9.65 (1H, br)

10) 4-[2-(3-Acetylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.48-1.92 (6H, m), 1.91 (3H, s), 1.96-2.25 (2H, m), 2.30 (3H, s), 2.30-2.39 (2H, m), 2.68 (6H, s), 3.32 (3H, s), 3.35-3.47 (2H, m), 3.76 (3H, s), 4.26 (2H, br), 4.75 (1H, br), 6.56-7.12 (6H, m), 7.47 (1H, br), 8.10 (1H, br), 8.39 (1H, br)

11) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(3-aminopropionyl)aminobut-1-yl]oxy-4-methylphenyl]-N-methylbenzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.59-1.90 (4H, m), 2.04-2.15 (2H, m), 2.27 (3H, s), 2.30-2.44 (2H, m), 2.87-3.08 (4H, m), 3.21-3.38 (2H, m), 3.30 (3H, s), 3.75-3.94 (2H, m), 3.76 (3H, s), 4.21-4.33 (2H, m), 6.55-6.68 (2H, m), 6.86-7.10 (5H, m), 7.29-7.48 (2H, m), 8.17 (1H, br), 8.35 (1H, br)

12) 4-[2-(3-Guanidinoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.49-1.93(6H, m), 2.05-2.41 (8H, m), 2.27 (3H, s), 2.75 (6H, s), 3.08 (2H, br), 3.29 (3H, s), 3.47 (2H, br), 3.67-4.10 (4H, m), 3.77 (3H, s), 4.27 (2H, br), 6.56-6.71 (2H, m), 6.81-7.09 (5H, m), 7.44 (1H, br), 7.98-8.19 (2H, m), 8.28-8.45 (1H, m)

13) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.35-1.66 (4H, m), 1.66-1.83 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7Hz), 2.74 and 2.76 (total 3H, s), 2.80-3.10 (4H, m), 3.18 (3H, s), 3.28-3.63 (2H, m), 3.68 (3H, s), 3.77-4.18 (3H, m), 4.34-4.52 (1H, m), 6.64 (1H, d, J=9Hz), 6.75-7.12 (6H, m), 7.40 (1H, m), 7.98 (1H, d, J=9Hz), 8.23 (1H, d, J=9Hz)

14) (S)-4-[2-[(3-Amino-1-methylprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.35 (3H, d, J=7Hz), 1.40-1.65 (4H, m), 1.66-1.82 (2H, m), 1.92-2.20 (2H, m), 2.23 (3H, s), 2.38 (2H, t, J=7Hz), 2.64 (3H, s), 2.78-3.43 (11H, m), 3.51-4.07 (7H, m), 4.93-5.09 (1H, m), 6.65 (1H, d, J=8Hz), 6.82 (1H, s), 6.89 (1H, d, J=8Hz), 6.98 (1H, s), 7.04 (1H, d, J=8Hz), 7.12 (1H, dd, J=8, 8Hz), 7.36 (1H, d, J=8Hz), 7.57 (1H, dd, J=8, 8Hz), 7.98-8.35 (4H, m)

15) 4-(2-Aminobenzenesulfonyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.36-1.45 (2H, m), 1.50-1.59 (2H, m), 1.65-1.73 (2H, m), 2.23 and 2.29 (total 3H, s), 2.34-2.42 (4H, m), 2.77 (3H, d, J=1Hz), 2.92-3.00 (2H, m), 3.11 and 3.13 (total 3H, s), 3.19 (1H, s), 3.36-3.70 (10H, m), 4.03-4.11 (1H, m), 4.40-4.48 (1H, m), 6.44-6.50 (1H, m), 6.60-6.88 (6H, m), 6.94-7.10 (2H, m), 7.27-7.32 (1H, m)

ESI-MASS (m/z) : 638 (M+H)

16) (R)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.37 and 1.39 (total 3H, s), 1.40-1.78 (8H, m), 1.94-2.12 (3H, m), 2.23 (3H, s), 2.30-2.40 (4H, m), 2.87-2.96 (2H, m), 3.18 (3H, s), 3.32 (3H, s), 3.46-3.58 (2H, m), 3.77 (3H, s), 3.83-3.99 (3H, m), 4.94-5.02 (1H, m), 6.65 (1H, d, J=8Hz), 6.82 (1H, s), 6.88 (1H, d, J=8Hz), 6.98 (1H, s), 7.03 (1H, d, J=8Hz), 7.13 (1H, t, J=8Hz), 7.33 (1H, d, J=9Hz), 7.58 (1H, t, J=8Hz), 7.88-8.02 (2H, br), 8.04 (1H, d, J=9Hz), 8.27 (1H, d, J=8Hz)
ESI-MASS (m/z) : 674 (M+H)

17) (R)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5- (4-dimethylaminopiperidin-1-yl) carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.36 and 1.38 (total 3H, s), 1.40-1.80 (12H, m), 1.88-2.13 (3H, m), 2.24 (3H, s), 2.35 (2H, t, J=8Hz), 2.51 (6H, s), 2.89-3.03 (4H, m), 3.19 (3H, s), 3.76 (3H, s), 3.83-4.00 (3H, m), 4.43-4.51 (1H, m), 4.96-5.03 (1H, m), 6.65 (1H, d, J=8Hz), 6.83 (1H, s), 6.87-6.92 (1H, m), 6.98 (1H, s), 7.03 (1H, d, J=8Hz), 7.14 (1H, t, J=8Hz), 7.34 (1H, d, J=8Hz), 7.58 (1H, t, J=8Hz), 8.04 (1H, d, J=8Hz), 8.24-8.30 (1H, m)
ESI-MASS (m/z) : 702 (M+H)

18) (S)-4-[2-[(4-Aminobut-2-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.35 and 1.38 (total 3H, s), 1.42-1.79 (12H, m), 1.88-2.14 (3H, m), 2.25 (3H, s), 2.36 (2H, t, J=8Hz), 2.51 (6H, s), 2.89-3.02 (4H, m), 3.20 (3H, s), 3.76 (3H, s), 3.84-4.00 (3H, m), 4.43-4.50 (1H, m), 4.97-5.03 (1H, m), 6.65 (1H, d, J=8Hz), 6.82 (1H, s), 6.88-6.92 (1H, m), 6.98 (1H, s), 7.02 (1H, d, J=8Hz), 7.15 (1H, t, J=8Hz), 7.34 (1H, d, J=8Hz), 7.58 (1H, t, J=8Hz), 8.03 (1H, d, J=8Hz), 8.24-8.30 (1H, m)
ESI-MASS (m/z) : 702 (M+H)

19) 4-[2-(4-Aminobut-1-yl)oxybenzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide dihydrochloride
NMR (D_2O, δ) : 1.35-1.50 (2H, m), 1.56-1.64 (2H, m), 1.68-1.83 (4H, m), 2.47 (2H, t, J=7.5Hz), 2.82-3.12 (5H, m), 2.92 (3H, s), 3.33 (3H, s), 3.43-3.61 (3H, m), 3.81 (1H, m), 3.95 (1H, m), 6.84 (1H, d, J=7Hz), 6.91 (1H, t, J=7Hz), 7.00-7.08 (3H, m), 7.19 (1H, t, J=7Hz), 7.26-7.37 (4H, m), 7.48 (1H, t, J=7Hz), 7.62 (1H, d, J=7Hz)

20) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methyl-benzamide hydrochoiride
NMR (DMSO-d_6, δ) : 1.16 (3H, t, J=7.5Hz), 1.38-1.49 (2H, m), 1.55-1.64 (2H, m), 1.67-1.77 (2H, m), 1.98-2.08 (2H, m), 2.21 (3H, s), 2.31 (2H, t, J=7.5Hz), 2.87-2.97 (2H, m), 3.16 (3H, s), 3.80-3.98 (2H, m), 4.03 (2H, q, J=7.5Hz), 4.19 (2H, t, J=7.5Hz), 6.62 (1H, d, J=7Hz), 6.80 (1H, s), 6.98-7.07 (2H, m), 7.15 (1H, d, J=7Hz), 7.22 (2H, d, J=8Hz), 7.43-7.57 (4H, m), 7.86-8.00 (3H, br)

21) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.38-1.49 (2H, m), 1.52-1.62 (2H, m), 1.68-1.78 (2H, m), 1.96-2.09 (2H, m), 2.21 (3H, s), 2.38 (2H, t, J=7.5Hz), 2.73 (3Hx1/2, s), 2.75 (3Hx1/2, s), 2.81-3.07 (4H, m), 3.15 (3H, s), 3.30-3.54 (4H, m), 3.81-4.21 (5H, m), 4.45 (1H, m), 6.65 (1H, d, J=7Hz), 6.81 (1H, s), 6.99-7.08 (2H, m), 7.15 (1H, d, J=7Hz), 7.22 (2H, d, J=8Hz), 7.45-7.60 (4H, m), 8.04 (2H, br)

22) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylprop-1-yl]oxy]-phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.90-2.09 (4H, m), 2.48-2.59 (2H, m), 2.72 (3Hx1/2, s), 2.73 (3Hx1/2, s), 2.83-3.10 (4H, m), 3.20 (3H, s), 3.33-3.56 (3H, m), 3.88-4.09 (3H, m), 4.18 (2H, t, J=7.5Hz), 4.47 (1H, m), 4.80 (1H, m), 6.87 (1H, t, J=7Hz), 6.98 (1H, d, J=7Hz), 7.04 (1H, t, J=7Hz), 7.11-7.26 (5H, m), 7.44-7.59 (4H, m), 8.05 (2H, br)

23) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-(4-methylpiperazin-1-ylcarbonyl)phenyl-methoxy]-phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.97-2.07 (2H, m), 2.26 (3H, s), 2.75 (3Hx1/2, s), 2.77 (3Hx1/2, s), 2.82-2.95 (2H, m), 3.02-3.14 (2H, m), 3.21 (3H, s), 3.30-3.49 (4H, m), 3.97-4.21 (4H, m), 5.09 (1H, d, J=14Hz), 5.20 (1H, d, J=14Hz), 6.70 (1H, d, J=7Hz), 6.93 (1H, s), 7.02-7.25 (5H, m), 7.43-7.57 (8H, m), 7.92-8.04 (3H, br)

24) 4-[2-(3-Hydroxyprop-1-yl)oxybenzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.39-1.50 (2H, m), 1.52-1.62 (2H, m), 1.69-1.79 (2H, m), 1.84-1.93 (2H, m), 2.40 (2H, t, J=7.5Hz), 2.70 (3Hx1/2, s), 2.72 (3Hx1/2, s), 2.82-3.07 (4H, m), 3.19 (3H, s), 3.28-3.60 (4H, m), 3.80-3.98 (2H, m), 4.10 (1H, m), 4.17 (2H, t, J=7.5Hz), 4.45 (1H, m), 6.85 (1H, t, J=7Hz), 6.98 (1H, d, J=7Hz), 7.03 (1H, t, J=7Hz), 7.13-7.24 (5H, m), 7.43-7.54 (3H, m), 7.62 (1H, d, J=7Hz)

25) 4-[2-(4-Hydroxy-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.42-1.52 (2H, m), 1.54-1.64 (2H, m), 1.70-1.82 (2H, m), 2.37-2.47 (6H, m), 2.49 (3H, s), 2.51 (3H, s), 2.84-3.05 (2H, m), 3.32-3.46 (4H, m), 3.84-3.98 (2H, m), 4.08 (1H, m), 4.47 (1H, m), 6.84 (1H, t, J=7Hz), 6.97 (1H, d, J=7Hz), 7.13-7.25 (4H, m), 7.41-7.53 (6H, m)

26) 4-[2-(4-Aminobut-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.39-1.62 (8H, m), 1.67-1.80 (2H, m), 2.39 (3H, t, J=7.5Hz), 2.50 (3H, s), 2.63-2.73 (4H, m), 2.81-3.08 (2H, m), 3.18 (3H, s), 3.31-3.42 (4H, m), 3.85-4.00 (2H, m), 4.04 (1H, m), 4.43 (1H, m), 6.84 (1H, t, J=7Hz), 6.99 (1H, d, J=7Hz), 7.11-7.42 (6H, m), 7.50-7.56 (2H, m), 7.75-7.91 (2H, m)

27) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yl]oxy]phenylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.40-1.51 (2H, m), 1.53-1.62 (2H, m), 1.69-1.80 (2H, m), 1.98 (3H, s), 1.98-2.03 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7.5Hz), 2.71 (3Hx1/2, s), 2.74 (3Hx1/2, s), 2.83-3.05 (2H, m), 3.31-3.50 (3H, m), 3.56 (2H, t, J=7.5Hz), 3.72 (3H, s), 3.81-4.11 (5H, m), 4.32 (2H, t, J=7.5Hz), 4.43 (1H, m), 6.65 (1H, d, J=7Hz), 6.81 (1H, s), 6.87-6.95 (2H, m), 7.05 (1H, d, J=7Hz), 7.11 (1H, t, J=7Hz), 7.26 (1H, d, J=7Hz), 7.54 (1H, t, J=7Hz), 8.03 (1H, d, J=7Hz), 8.28 (1H, d, J=7Hz)

28) 3-Methoxy-4-(2-hydroxybenzoyl)amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenylmethoxy]phenylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 2.23 (3H, s), 2.75 (3Hx1/2, s), 2.77 (3Hx1/2, s), 2.97-3.15 (2H, m), 3.21 (3H, s), 3.24-3.80 (6H, m), 5.06 (1H, d, J=14Hz), 5.19 (1H, d, J=14Hz), 6.70 (1H, d, J=7Hz), 6.90-7.01 (3H, m), 7.10 (1H, d, J=7Hz), 7.22 (2H, d, J=8Hz), 7.41 (1H, d, J=7Hz), 7.44-7.55 (7H, m), 7.87 (1H, d, J=7Hz)

29) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 2.06-2.19 (2H, m), 2.23 (3H, s), 2.75 (3H, s), 2.87-2.98 (2H, m), 3.02-3.15 (2H, m), 3.23 (3H, s), 3.32-3.49 (2H, m), 3.65 (3H, s), 3.71-3.96 (4H, m), 4.29-4.40 (2H, m), 5.04 (1H, d, J=14Hz), 5.20 (1H, d, J=14Hz), 6.76 (1H, d, J=7Hz), 6.88 (1H, d, J=7Hz), 6.90-6.98 (2H, m), 7.09-7.19 (2H, m), 7.28 (1H, d, J=7Hz), 7.50-7.62 (2H, m), 7.98-8.15 (4H, m), 8.23 (1H, d, J=7Hz)

30) 3-Methoxy-4-[2-(3-aminoprop-1-yl)cxy]phenylmethyl]-amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide trihydrochloride
NMR (DMSO-d_6, δ) : 1.35-1.47 (2H, m), 1.49-1.59 (2H, m), 1.64-1.74 (2H, m), 2.00-2.10 (2H, m), 2.22 (3H, s), 2.30-2.38 (2H, m), 2.69 (3Hx1/2, s), 2.73 (3Hx1/2, s), 2.82-3.03 (6H, m), 3.09 (3H, s), 3.29-3.41 (2H, m), 3.53 (3H, s), 3.83-4.12 (6H, m), 4.22 (2H, s), 4.70 (1H, br), 6.21 (1H, d, J=7Hz), 6.58-6.66 (2H, m), 6.71-6.99 (5H, m), 7.09 (1H, d, J=7Hz), 7.20 (1H, t, J=7Hz), 8.02 (2H, br d)

31) 4- (2-Dimethylamino-4-methyl)phenoxymethyl-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.37-1.47 (2H, m), 1.50-1.61 (2H, m), 1.67-1.80 (2H, m), 2.20 (3H, s), 2.29 (3H, s), 2.39 (2H, t, J=7.5Hz), 2.71 (3Hx1/2, s), 2.73 (3Hx1/2, s), 2.80-3.58 (4H, m), 3.03 (6H, s), 3.17 (3H, s), 3.72-4.48 (6H, m), 5.21 (2H, s), 6.62 (1H, d, J=7Hz), 6.78 (1H, s), 6.91 (1H, d, J=7Hz), 7.02 (1H, d, J=7Hz), 7.11 (1H, d, J=7Hz), 7.26 (2H, d, J=8Hz), 7.37 (2H, d, J=8Hz), 7.70 (1H, d, J=7Hz)

32) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenyleth-1-yl]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 2.06-2.19 (2H, m), 2.55-3.12 (10H, m), 2.71 (3Hx1/2, s), 2.73 (3Hx1/2, s), 3.18 (3H, s), 3.23-3.48 (2H, m), 3.66 (3H, s), 3.66-3.81 (2H, m), 4.30-4.40 (2H, m), 6.86-6.90 (2H, m), 7.11 (1H, t, J=7Hz),

7.20-7.42 (9H, m), 7.59 (1H, t, J=7Hz), 8.01 (1H, d, J=7Hz), 8.08 (2H, br), 8.27 (1H, d, J=7Hz)

33) 4-[2-(3-Aminoprop-1-yl)thiobenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.40-1.51 (3H, m), 1.52-1.63 (2H, m), 1.70-1.88 (4H m), 2.23 (3H, s), 2.40 (3H, t, J=7.5Hz), 2.71 (3Hx1/2, s), 2.72 (3Hx1/2, s), 2.80-2.91 (2H, m), 2.94-3.06 (2H, m), 3.17 (3H, s), 3.32-3.67 (8H, m), 3.60 (3H, s), 3.81-4.10 (3H, m), 4.41 (1H, m), 6.65 (1H, d, J=7Hz), 6.82 (1H, s), 6.86-6.92 (2H, m), 7.02 (1H, d, J=7Hz), 7.27 (1H, t, J=7Hz), 7.41-7.52 (3H, m), 7.71 (1H, d, J=7Hz), 9.37 (1H, s)

34) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(4-dimethylaminopiperidin-1-yl)carbonyl]phenylmethoxy-4-methyl]phenyl-N-methylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.57-1.73 (2H, m), 2.00-2.20 (4H, m), 2.23 (3H, s), 2.70 (3H, s), 2.71 (3H, s), 2.87-3.05 (3H, m), 3.24 (3H, s), 3.33-3.50 (1H, m), 3.66 (3H, s), 3.71-4.05 (4H, m), 4.37 (2H, t, J=7.5Hz), 5.02 (1H, d, J=14Hz), 5.20 (1H, d, J=14Hz), 6.73 (1H, d, J=7Hz), 6.86 (1H, d, J=7Hz), 6.96 (2H, s), 7.10-7.19 (2H, m), 7.29 (1H, d, J=7Hz), 7.43-7.52 (4H, m), 7.58 (1H, t, J=7Hz), 8.00 (1H, d, J=7Hz), 8.03 (1H, d, J=7Hz)

35) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonyl-methoxyprop-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.94-2.04 (2H, m), 2.10-2.20 (2H, m), 2.71 (3Hx1/2, s), 2.23 (3Hx1/2, s), 2.84-3.10 (6H, m), 3.21 (3H, s), 3.31-3.50 (2H, m), 3.57-3.81 (4H, m), 3.74 (3H, s), 3.90-4.01 (2H, m), 4.20 (2Hx1/2, s), 4.22 (2Hx1/2, d), 4.35 (2H, t, J=7.5Hz), 6.82-6.97 (3H, m), 7.01 (1H, d, J=7Hz), 7.10-7.28 (4H, m), 7.58 (1H, t, J=7Hz), 8.03 (1H, d, J=7Hz), 8.27 (1H, d, J=7Hz)

36) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[(E)-5-(4-dimethylaminopiperidin-1-yl)carbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.36-1.63 (2H, m), 1.84-1.92 (2H, m), 1.97-2.08 (2H, m), 2.10-2.22 (2H, m), 2.22 (3H, s), 2.29-2.43 (2H, m), 2.63 (3H, s), 2.65 (3H, s), 2.70-2.86 (2H, m), 2.88-3.00 (2H, m), 3.14 (3Hx1/2, s), 3.17 (3Hx1/2, s), 3.28-3.42 (2H, m), 3.71 (3H, s), 3.84-4.06 (2H, m), 4.37 (2H, t, J=7.5Hz), 4.51 (1H, m), 6.52 (1H, d, J=15Hz), 6.60 (1H, m), 6.73-7.07 (5H, m), 7.13 (1H, t, J=7Hz), 7.27 (1H, d, J=7Hz), 7.56 (1H, t, J=7Hz), 8.01 (1H, d, J=7Hz), 8.30 (1H, d, J=7Hz)

37) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperidin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide hydrochloride
NMR ($CDCl_3$, δ) : 0.88 (3H, d, J=7.5Hz), 0.90-1.10 (2H, m), 1.34-1.61 (6H, m), 1.70-1.80 (2H, m), 2.10-2.20 (2H, m), 2.23 (3H, s), 2.30 (2H, t, J=7.5Hz), 2.45 (1H, m), 2.85-3.00 (3H, m), 3.18 (3H, s), 3.74 (3H, s), 3.75-4.02 (4H, m), 4.38 (2H, t, J=7.5Hz), 4.78 (1H, m), 6.65 (1H, d, J=7Hz), 6.82 (1H, s), 6.88 (1H, d, J=7Hz), 6.98 (1H, s), 7.02 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz), 7.26 (1H, d, J=7Hz), 7.59 (1H, t, J=7Hz), 8.00 (1H, d, J=7Hz), 8.22 (1H, d, J=7Hz)

38) 4-(2,4-Dimethoxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.40-1.51 (2H, m), 1.51-1.64 (2H, m), 1.69-1.82 (2H, m), 2.22 (3H, s), 2.38 (2H, t, J=7.5Hz), 2.73 (3H, s), 2.81-3.09 (4H, m), 3.19 (3H, s), 3.25-3.50 (2H, m), 3.76 (6H, sx2), 3.77-4.15 (3H, m), 4.00 (3H, s), 4.44 (1H, m), 6.64 (1H, d, J=7Hz), 6.81 (1H, s), 6.88-6.95 (2H, m), 7.03 (1H, d, J=7Hz), 7.12-7.23 (2H, m), 7.57 (1H, m), 8.29 (1H, d, J=7Hz)

39) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(3-aminoprop-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 2.00-2.11 (2H, m), 2.13-2.20 (2H, m), 2.25 (3H, s), 2.87-3.00 (4H, m), 3.19 (3H, s), 3.77 (3H, s), 3.89-4.10 (2H, m), 4.36 (2H, t, J=7.5Hz), 6.69 (1H, d, J=7Hz), 6.82 (1H, s), 6.89 (1H, d, J=7Hz), 7.04 (1H, s), 7.05 (1H, d, J=7Hz), 7.15 (1H, d, J=7Hz), 7.38 (1H, d, J=7Hz), 7.56 (1H, t, J=7Hz), 8.01 (1H, d, J=7Hz), 8.28 (1H, d, J=7Hz)

40) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-aminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.66-1.85 (4H, m), 2.10-2.20 (2H, m), 2.22 (3H, s), 2.80-3.01 (4H, m), 3.18 (3H, s), 3.75 (3H, s), 3.81-4.03 (2H, m), 4.36 (2H, t, J=7.5Hz), 6.64 (1H, d, J=7Hz), 6.34 (1H, s), 6.90 (1H, d, J=7Hz), 6.96 (1H, s), 7.01 (1H, d, J=7Hz), 7.14 (1H, t, J=7Hz), 7.27 (1H, d, J=7Hz), 7.57 (1H, t, J=7Hz), 8.00 (1H, d, J=7Hz), 8.25 (7H,

d, J=7Hz)

41) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-acetylaminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.49-1.59 (2H, m), 1.67-1.77 (2H, m), 1.80 (3H, s), 2.06-2.20 (2H, m), 2.21 (3H, s), 2.86-3.00 (2H, m), 3.03-3.13 (2H, m), 3.18 (3H, s), 3.74 (3H, s), 3.80-4.02 (2H, m), 4.35 (2H, t, J=7.5Hz), 6.64 (1H, d, J=7Hz), 7.82 (1H, s), 7.88 (1H, d, J=7Hz), 7.96 (1H, s), 7.02 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz), 7.26 (1H, d, J=7Hz), 7.57 (1H, t, J=7Hz), 8.00 (1H, d, J=7Hz), 8.23 (1H, d, J=7Hz)

42) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-aminoacetylaminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.53-1.64 (2H, m), 1.70-1.81 (2H, m), 2.09-2.21 (2H, m), 2.22 (3H, s), 2.86-2.98 (2H, m), 3.11-3.23 (2H, m), 3.17 (3H, s), 3.47-3.56 (2H, m), 3.65-4.00 (2H, m), 3.76 (3H, s), 4.38 (2H, t, J=7.5Hz), 6.65 (1H, d, J=7Hz), 6.82 (1H, s), 6.89 (1H, d, J=7Hz), 6.95 (1H, s), 7.03 (1H, d, J=7Hz), 7.12 (1H, t, J=7Hz), 7.25 (1H, d, J=7Hz), 7.56 (1H, t, J=7Hz), 8.00 (1H, d, J=7Hz) 8.22 (1H, d, J=7Hz)

43) 3-Methoxy-4-[2-(piperidin-4-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.38-1.49 (2H, m), 1.49-1.61 (2H, m), 1.66-1.76 (2H, m), 1.85-1.97 (2H, m), 2.20 (3H, s), 2.67 (2H, t, J=7.5Hz), 2.73 (3Hx1/2, s), 2.74 (3Hx1/2, s), 2.80-3.13 (6H, m), 3.13 (3H, s), 3.22-3.51 (6H, m), 3.60-4.13 (3H, m), 3.74 (3H, s), 4.43 (1H, m), 4.91 (1H, m), 6.65 (1H, d, J=7Hz), 6.81 (1H, s), 6.89 (1H d, J=7Hz), 6.96 (1H, s), 7.03 (1H, d, J=7Hz), 7.12 (1H, c, J=7Hz), 7.35 (1H, d, J=7Hz), 7.56 (1H, t, J=7Hz), 7.81 (1H, d, J=7Hz), 8.27 (1H, d, J=7Hz)

44) 4-[2-(3-Amino-1-methylprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.35 (3H, d, J=7.5Hz), 1.40-1.63 (4H, m), 1.67-1.80 (2H, m), 1.90-2.18 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7.5Hz), 2.71 (3Hx1/2, s), 2.74 (3Hx1/2, s), 2.80-3.09 (4H, m), 3.18 (3H, s), 3.30-3.52 (4H, m), 3.77 (3H, s), 3.83-4.18 (3H, m), 4.42 (1H, m), 5.01 (1H, m), 6.64 (1H, d, J=7Hz), 6.81 (1H, s), 6.89 (1H, d, J=7Hz), 6.96 (1H, s), 7.03 (1H, d, J=7Hz), 7.12 (1H, t, J=7Hz), 7.34 (1H, d, J=7Hz), 7.58 (1H, t, J=7Hz), 8.03 (1H, d, J=7Hz), 8.28 (1H, d, J=7Hz)

45) 3-Methoxy-4-[2-(pyrid-3-yl)methoxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.36-1.49 (2H, m), 1.49-1.60 (2H, m), 1.66-1.79 (2H, m), 2.20 (3H, s), 2.39 (2H, t, J=7.5Hz), 2.68 (3Hx1/2, s), 2.70 (3Hx1/2, s), 2.80-3.10 (4H, m), 3.16 (3H, s), 3.35 (3H, s), 3.35-3.60 (2H, m), 3.79-4.11 (3H, m), 4.41 (1H, m), 5.58 (2H, s), 6.64 (1H, d, J=7Hz), 6.80-6.90 (3H, m), 7.02 (1H, d, J=7Hz), 7.16 (1H, t, J=7Hz), 7.33 (1H, d, J=7Hz), 7.57 (1H, t, J=7Hz), 7.93-8.00 (2H, m), 8.19 (1H, d, J=7Hz), 8.55 (1H, d, J=7Hz), 8.88 (1H, d, J=6Hz), 9.04 (1H, s)

46) 4-[2-(4-Aminobut-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.40-1.50 (2H, m), 1.50-1.61 (2H, m), 1.66-1.79 (4H, m), 1.86-1.95 (2H, m), 2.21 (3H, s), 2.39 (2H, t, J=7.5Hz), 2.73 (3Hx1/2, s), 2.75 (3Hx1/2, s), 2.79-3.10 (4H, m), 3.19 (3H, s), 3.31-3.52 (4H, m), 3.74 (3H, s), 3.82-4.12 (3H, m), 4.30 (2H, t, J=7.5Hz), 4.43 (1H, m), 6.65 (1H, d, J=7Hz), 7.81 (1H, s), 6.89 (1H, d, J=7Hz), 6.97 (1H, s), 7.03 (1H, d, J=7Hz), 7.12 (1H, t, J=7Hz), 7.30 (1H, d, J=7Hz), 7.58 (1H, d, J=7Hz), 8.04 (1H, d, J=7Hz), 8.30 (1H, d, J=7Hz)

47) 4-(2-Hydroxy-5-methylbenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.53-1.96 (6H, m), 2.29 (3H, s), 2.31 (3H, s), 2.33-2.40 (2H, m), 2.79 (3H, s), 3.30 (3H, s), 3.79 (3H, s), 3.80-4.03 (2H, m), 6.63 (2H, br), 6.88-6.98 (4H, m), 7.25 (1H, d, J=8Hz), 8.19 (1H, d, J=8Hz), 8.71 (1H, br)

48) 4-(2-Hydroxy-4-methoxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.48-1.92 (6H, m), 2.28 (3H, s), 2.32-2.45 (2H, m), 2.64-3.05 (4H, m), 2.79 (3H, s), 3.29 (3H, s), 3.29-3.51 (4H, m), 3.76 (3H, s), 3.80 (3H, s), 3.81-4.05 (4H, m), 6.43-6.50 (2H, m), 6.61 (1H, br), 6.85-6.96 (3H,

m), 7.36-7.43 (1H, m), 8.12-8.18 (1H, m), 8.58 (1H, br)

Example 18

[0332] The following compounds were obtained by separating the compounds, which were prepared according to a similar manner to Example 4, by using silica gel column chromatography.

1) 4-(2-Benzyloxy)benzoylamino-3-methoxy-N-[(E)-2-(4-carboxyphenyl)ethen-1-yl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.08 (3H, s), 3.41 (3H, s), 5.19 (2H, s), 6.47 (1H, d, J=14Hz), 6.58 (1H, d, J=14Hz), 6.73 (2H, d, J=8Hz), 6.84 (1H, d, J=7Hz), 6.90-7.10 (5H, m), 7.20-7.40 (8H, m), 7.71 (2H, d, J=8Hz), 8.26 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

2) 4-(2-Benzyloxy)benzoylamino-3-methoxy-N-[(Z)-2-(4-carboxyphenyl)ethen-1-yl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 3.09 (3H, s), 3.48 (3H, s), 5.25 (2H, s), 6.72-7.42 (15H, m), 7.51-7.64 (3H, m), 8.10 (2H, d, J=8Hz), 8.22 (1H, d, J=7Hz), 8.33 (1H, d, J=7Hz)

Example 19

[0333] The following compound was obtained according to a similar manner to that of Example 4 by using 4-[2-(acetoxy)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide as a starting compound.

4-[2-(Hydroxy)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-(5-carboxypent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.61 (2H, m), 1.63-1.90 (4H, m), 2.28 (3H, s), 2.39 (2H, t, J=7Hz), 3.33 (3H, s), 3.73-4.00 (5H, m), 6.61 (2H, br s), 6.82-7.11 (5H, m), 7.35-7.53 (2H, m), 8.16 (1H, d, J=8Hz), 8.75 (1H, br s)

Example 20

[0334] The following compounds were obtained according to a similar manner to that of Example 8.

1) 4-[2-(4-Methoxybenzyl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.31 (3H, s), 2.35-2.53 (4H, m), 3.32 (3H, s), 3.39-3.54 (2H, m), 3.67-3.85 (3H, m), 3.82 (3H, s), 4.95 (1H, d, J=14Hz), 5.06 (1H, d, J=14Hz), 5.12 (2H, s), 6.59-6.67 (2H, m), 6.86-7.02 (5H, m), 7.07-7.21 (4H, m), 7.33-7.52 (7H, m), 8.28 (1H, d, J=7Hz)

2) 4-(2-Benzyloxybenzoyl)amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.46-1.60 (2H, m), 1.63-1.92 (4H, m), 2.30 (3H, s), 2.31-2.46 (6H, m), 3.28 (3H, s), 3.35 (3H, s), 3.44-3.54 (2H, m), 3.58-3.69 (2H, m), 3.80-4.04 (2H, m), 5.30 (2H, s), 6.73-7.22 (8H, m), 7.30-7.49 (6H, m), 8.19-8.28 (1H, m), 8.38 (1H, d, J=9Hz)

3) 4-[2-(Benzyloxy)benzoyl]amino-2-chloro-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.48-1.65 (2H, m), 1.65-1.97 (4H, m), 2.30 (3H, s), 2.32-2.48 (6H, m), 3.34 (3H, s), 3.43-3.56 (2H, m), 3.58-3.70 (2H, m), 3.97 (2H, t, J=7Hz), 5.16 (2H, s), 6.63-6.81 (3H, m), 6.96 (1H, d, J=8Hz), 7.02-7.20 (5H, m), 7.40-7.59 (6H, m), 8.24 (1H, m)

4) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.42 (9H, s), 1.45-1.82 (8H, m), 2.10-2.19 (2H, m), 2.30 (3H, s), 2.31-2.41 (6H, m), 3.27-3.35 (2H, m), 3.43-3.50 (5H, m), 3.60-3.67 (2H, m), 3.82 (3H, s), 3.90 (1H, t, J=7Hz), 4.27 (1H, t, J=7Hz), 4.75-4.82 (1H, br), 6.76 (2H, d, J=8Hz), 6.82 (1H, d, J=8Hz), 6.95-7.04 (3H, m), 7.07-7.13 (1H, m), 7.47 (1H, t, J=8Hz), 8.22 (1H, dd, J=1, 8Hz), 8.42 (1H, d, J=8Hz)
ESI-MASS (m/z) : 746 (M+H)

5) 4-[2-[3-(tert-Butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]-amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.60 (2H, m), 1.65-1.74 (2H, m), 1.78-1.89 (2H, m), 2.04-2.15 (2H, m), 2.27

(3H, s), 2.30 (3H, s), 2.32-2.42 (6H, m), 3.27-3.39 (2H, m), 3.33 (3H, s), 3.44-3.50 (2H, m), 3.58-3.64 (2H, m), 3.82-4.00 (2H, m), 4.19 (2H, t, J=7.5Hz), 4.86 (1H, br), 6.55-6.62 (2H, m), 6.86 (1H, d, J=7Hz), 6.97 (1H, d, J=7Hz), 7.08 (1H, t, J=7Hz), 7.31 (2H, d, J=8Hz), 7.40-7.53 (3H, m), 8.13 (1H, d, J=7Hz), 9.88 (1H, s)

6) 4-(2-Iodobenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.43-1.54 (2H, m), 1.61-1.70 (2H, m), 1.74-1.86 (2H, m), 2.28 (3H, s), 2.28-2.41 (6H, m), 3.34 (3H, s), 3.44-3.50 (2H, m), 3.52-3.59 (2H, m), 3.73-3.99 (2H, m), 6.77-6.84 (2H, m), 7.03 (1H, d, J=7Hz), 7.10-7.19 (2H, m), 7.29-7.50 (5H, m), 7.80 (1H, s), 7.89 (1H, d, J=7Hz)

7) 4-(2-Dimethylamino-4-methyl)phenoxymethyl-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.47-1.58 (2H, m), 1.64-1.75 (2H, m), 1.77-1.88 (2H, m), 2.22 (3H, s), 2.25 (3H, s), 2.28 (3H, s), 2.31-2.41 (6H, m), 2.72 (6H, s), 3.32 (3H, s), 3.43-3.51 (2H, m), 3.58-3.67 (2H, m), 3.79-3.97 (2H, m), 5.02 (2H, s), 6.49-6.61 (3H, m), 6.71 (1H, d, J=7Hz), 7.80-7.85 (2H, m), 7.19 (2H, d, J=8Hz), 7.28 (2H, d, J=8Hz)

8) 4-(2-Benzyloxy)benzoylamino-3-methoxy-N-methyl-N-[(E)-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylethen-1-yl]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.11-2.40 (4H, m), 2.17 (3H, s), 3.11 (3H, s), 3.18-3.38 (2H, m), 3.44 (3H, s), 3.49-3.68 (2H, m), 5.27 (2H, s), 6.41 (1H, d, J=14Hz), 6.56 (1H, d, J=14Hz), 6.70 (2H, d, J=8Hz), 6.88-7.48 (16H, m), 8.26 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

9) 3-Methoxy-4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperidin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 0.93 (3H, d, J=7.5Hz), 0.98-1.14 (2H, m), 1.40 (9H, s), 1.42-1.87 (8H, m), 2.07-2.17 (2H, m), 2.25 (3H, s), 2.32 (2H, t, J=7.5Hz), 2.50 (1H, m), 2.97 (1H, m), 3.21-3.32 (2H, m), 3.32 (1H, s), 3.79 (1H, s), 3.79-4.00 (4H, m), 4.24 (2H, t, J=7.5Hz), 4.55 (1H, m), 4.84 (1H, m), 6.59 (1H, d, J=7Hz), 6.63 (1H, s), 6.85 (1H, d, J=7Hz), 6.92 (1H, d, J=7Hz), 6.95-7.13 (3H, m), 7.45 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

10) 3-Methoxy-4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-N-[2-[5-[(2S)-carbamoylpyrrolidin-1-yl]carbonylpent-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.28-2.20 (12H, m), 1.39 (9H, s), 2.27 (3H, s), 3.19-3.25 (2H, m), 3.21 (3H, s), 3.25-3.61 (2H, m), 3.78 (3H, s), 3.81-4.03 (2H, m), 4.16-4.29 (2H, m), 4.57 (1H, m), 6.55-6.68 (2H, m), 6.80-7.13 (5H, m), 7.44 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

11) 3-Methoxy-4-[2-[1-(tert-butoxycarbonyl)piperidin-4-yl]-oxybenzoyl)amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.41-1.59 (2H, m), 1.46 (9H, s), 1.69-1.94 (6H, m), 2.00-2.13 (2H, m), 2.26 (3H, s), 2.29 (3H, s), 2.33-2.41 (8H, m), 2.96-3.17 (2H, m), 3.31 (3H, s), 3.45-3.51 (2H, m), 3.59-3.67 (2H, m), 3.74 (3H, s), 3.80-4.01 (2H, m), 4.68 (1H, m), 6.58-6.63 (2H, m), 6.85 (1H, d, J=7Hz), 6.90 (1H, d, J=7Hz), 6.99-7.11 (2H, m), 7.35-7.61 (2H, m), 8.19 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

12) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)amino-1-methylprop-1-yl]oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.30 (9H, s), 1.31 (3H, d, J=7.5Hz), 1.45-2.10 (8H, m), 2.27 (3H, s), 2.29 (3H, s), 2.32-2.43 (6H, m), 3.20-3.30 (2H, m), 3.32 (3H, s), 3.45-3.50 (2H, m), 3.60-3.66 (2H, m), 3.79 (3H, s), 3.82-4.00 (2H, m), 4.72 (1H, m), 6.60 (1H, d, J=7Hz), 6.64 (1H, s), 6.81-6.93 (2H, m), 7.00-7.11 (3H, m), 7.43 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.42 (1H, d, J=7Hz)

13) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-(5-aminocarbonylpent-1-yl)oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.42 (9H, s), 1.50-1.92 (6H, m), 2.12-2.26 (2H, m), 2.29 (2H, t, J=5Hz), 2.30 (3H, s), 3.30 (2H, q, J=5Hz), 3.35 (3H, s), 3.77 (3H, s), 3.80-4.02 (2H, m), 4.25 (2H, t, J=5Hz), 6.61-6.70 (2H, m), 6.93-7.15 (6H, m), 7.41-7.51 (1H, m), 8.20 (1H, d, J=7Hz), 8.42 (1H, d, J=7Hz)

14) 4-[2-[3-(tert-Butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-[4-(tert-butoxycarbonyl)piperazin-1-yl]carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.49 (9H, s), 1.50-1.90 (6H, m), 2.12-2.23 (2H, m), 2.30 (3H, s), 2.39 (2H, t, J=5Hz), 3.30 (2H, q, J=5Hz), 3.33 (3H, s), 3.35-3.42 (4H, m), 3.44 (4H, s), 3.55-3.62 (2H, m), 3.80 (3H, s), 3.85-4.06 (2H,

m), 4.24 (2H, t, J=5Hz), 4.93 (1H, br), 6.57-6.66 (2H, m), 6.85-7.13 (6H, m), 7.44-7.52 (1H, m), 8.20 (1H, d, J=7Hz), 8.41 (1H, d, J=7Hz)

15) 4-[2-[3-(tert-Butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-morpholin-4-yl) carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.50-1.88 (6H, m), 2.10-2.21 (2H, m), 2.30 (3H, s), 2.36 (2H, t, J=5Hz), 3.30 (2H, q, J=5Hz), 3.34 (3H, s), 3.47 (2H, t, J=4Hz), 3.58-3.70 (6H, m), 3.79 (3H, s), 3.84-4.03 (2H, m), 4.25 (2H, t, J=5Hz), 4.89 (1H, br), 6.56-6.68 (2H, m), 6.84-7.16 (6H, m), 7.41-7.51 (2H, m), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

16) 4-[2-[3-(tert-Butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-methylhomopiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.46-1.97 (8H, m), 2.09-2.21 (2H, m), 2.29 (3H, s), 2.32 (2H, t, J=5Hz), 2.33 (3H, s), 2.52-2.66 (4H, m), 3.30 (2H, q, J=5Hz), 3.33 (3H, s), 3.50-3.69 (4H, m), 3.79 (3H, s), 3.84-4.03 (2H, m), 4.24 (2H, t, J=5Hz), 4.94 (1H, br), 6.56-6.67 (2H, m), 6.82-7.12 (6H, m), 7.40-7.49 (1H, m), 8.20 (1H, d, J=7Hz), 8.41 (1H, d, J=8Hz)

17) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(2-dimethylaminoeth-1-yl)aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.42-1.59 (4H, m), 1.67-1.90 (4H, m), 1.97-2.32 (4H, m), 2.28 (3H, s), 2.34 (6H, s), 2.56 (2H, br), 3.25-3.42 (4H, m), 3.32 (2H, s), 3.50 (1H, s), 3.78-4.01 (2H, m), 3.80 (3H, s), 4.25 (2H, t, J=6Hz), 4.91 (1H, br), 6.52-6.76 (3H, m), 6.87-7.13 (7H, m), 7.45 (1H, m), 8.19 (1H, d, J=8Hz), 8.41 (1H, br)

18) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-[N-(3-dimethylamino-prop-1-yl)-N-methylcarbamoylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.50-1.96 (6H, m), 2.11-2.25 (2H, m), 2.27 (3H, s), 2.30-2.43 (2H, m), 2.50 (6H, s), 2.91 and 3.02 (total 3H, s, rotamer), 3.08 and 3.32 (total 2H, q, rotamer, J=5Hz), 3.33 (3H, s), 3.43 (2H, t, J=5Hz), 3.79 (3H, s), 3.83-4.02 (2H, m), 4.25 (2H, t, J=5Hz), 6.57-6.68 (2H, m), 6.82-7.13 (6H, m), 7.42-7.50 (1H, m), 8.21 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

19) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2- [5-[bis(2-hydroxyeth-1-yl)amino]carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.55-1.89 (6H, m), 2.11-2.20 (2H, m), 2.28 (3H, s), 2.40-2.56 (2H, m), 3.29 (2H, t, J=5Hz), 3.40-3.57 (4H, m), 3.68-4.02 (6H, m), 4.26 (2H, t, J=5Hz), 6.60-6.68 (2H, m), 6.90-7.15 (6H, m), 7.42-7.51 (1H, m), 8.19 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

20) 4-[2- (3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(2,2-dimethylhydrazino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR (DMSO-d_6, δ) : 1.40 (9H, s), 1.45-1.90 (6H, m), 2.08-2.20 (2H, m), 2.28 (3H, s), 2.30-2.45 (2H, m), 2.51 (3H, s), 2.60 (3H, s), 3.29 (2H, t, J=5Hz), 3.33 (3H, s), 3.75 (3H, s), 3.79-4.02 (2H, m), 4.25 (2H, t, J=5Hz), 6.57-6.68 (2H, m), 6.80-7.14 (5H, m), 7.41-7.50 (1H, m), 8.21 (1H, d, J=8Hz), 8.40-8.48 (1H, br)

21) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(carbamoylmethylamino)-carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.50-1.90 (6H, m), 2.12-2.19 (2H, m), 2.28 (3H, s), 2.53 (2H, t, J=5Hz), 3.30 (2H, t, J=5Hz), 3.33 (3H, s), 3.80 (3H, s), 3.84-3.99 (2H, m), 4.05 (2H, br), 4.25 (2H, t, J=5Hz), 4.84 (1H, br), 6.58-6.67 (2H, m), 6.72-7.12 (6H, m), 7.42-7.50 (1H, m), 8.18-8.23 (1H, m), 8.41 (1H, d, J=8Hz)

22) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(carbamoylethylamino)-carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.46-1.86 (6H, m), 2.12-2.25 (4H, m), 2.30 (3H, s), 2.41 (2H, t, J=5Hz), 3.30 (1H, q, J=5Hz), 3.37 (3H, s), 3.49 (1H, q, J=5Hz), 3.79 (3H, s), 3.82-4.03 (2H, m), 4.27 (2H, t, J=5Hz), 6.45-6.67 (4H, m), 6.88-7.15 (6H, m), 7.43-7.51 (1H, m), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

23) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-diethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.12 (6H, t, J=5Hz), 1.41 (9H, s), 1.42-1.92 (6H, m), 2.10-2.18 (2H, m), 2.27 (3H, s), 2.27-2.69 (9H, m), 3.26 (2H, t, J=5Hz), 3.31 (3H, s), 3.77 (3H, s), 3.87-4.02 (4H, m), 4.23 (2H, t, J=5Hz), 6.54-6.67 (2H, m), 6.72-7.15 (6H, m), 7.42-7.51 (1H, m), 8.19 (1H, d, J=8Hz), 8.42 (1H, d, J=8Hz)

24) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[3-(4-methylpiperazin-1-yl) carbonylpyrid-6-yl]methoxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.39 (9H, s), 2.06-2.18 (2H, m), 2.28 (3H, s), 2.31 (3H, s), 2.35-2.51 (4H, m), 3.27 (2H, q, J=5Hz), 3.38-3.49 (2H, m), 3.41 (1H, s), 3.63 (3H, s), 3.68-3.76 (2H, m), 4.21 (2H, t, J=5Hz), 4.97 (1H, d, J=12Hz), 5.14 (1H, d, J=12Hz), 6.58 (1H, s), 6.72 (1H, d, J=8Hz), 6.91-7.11 (7H, m), 7.20-7.25 (1H, m), 7.43 (1H, dd, J=2, 8Hz), 7.68 (1H, d, J=8Hz), 8.19 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz), 8.60 (1H, s)

25) 4- [2- (Benzyloxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.42 (2H, m), 1.48-1.58 (2H, m), 1.63-1.93 (6H, m), 2.29 (6H, s), 2.30-2.40 (3H, m), 2.50-2.60 (1H, m), 2.95-3.06 (1H, m), 3.29 (3H, s), 3.38 (3H, s), 3.80-4.00 (4H, m), 4.57-4.70 (1H, m), 5.30 (2H, s), 6.74-7.20 (9H, m), 7.32-7.45 (5H, m), 8.20-8.37 (1H, m), 8.37-8.42 (1H, m)

26) 4-[(2-Benzyloxy)benzoyl]amino-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylprop-1-yl]oxy]-phenybenzamide
NMR ($CDCl_3$, δ) : 2.05-2.16 (2H, m), 2.28 (3H, s), 2.32-2.40 (4H, m), 2.50 (2H, t, J=7.5Hz), 3.33 (3H, s), 3.43-3.50 (2H, m), 3.59-3.65 (2H, m), 3.88-4.05 (2H, m), 5.19 (2H, s), 6.77-6.84 (2H, m), 6.95-7.02 (3H, m), 7.09-7.20 (5H, m), 7.39-7.52 (6H, m), 8.27 (1H, d, J=7Hz)

Example 21

[0335] The following compounds were obtained according to similar manners to those of Examples 8 and 16.

1) 4-(6-Hydroxy-2-pyridylcarbonyl)amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.47-1.58 (2H, m), 1.64-1.73 (2H, m), 1.78-1.87 (2H, m), 2.27 (3H, s), 2.29 (3H, s), 2.28-2.41 (8H, m), 3.33 (3H, s), 3.45-3.51 (2H, m), 3.59-3.68 (6H, m), 3.86-3.94 (1H, br), 6.55-6.61 (2H, m), 6.86 (1H, d, J=8Hz), 7.30-7.38 (4H, m), 7.47-7.54 (2H, m), 8.06-8.10 (1H, m)
ESI-MASS (m/z) : 574 (M+H)

2) 4-[2-(Methoxy)benzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide hydrochloride
NMR (DMSO-d_6, δ) : 1.36-1.66 (4H, m), 1.66-1.83 (2H, m), 2.23 (3H, s), 2.39 (2H, t, J=7Hz), 2.74 (3H, s), 2.80-3.10 (3H, m), 3.17 (3H, s), 3.23-3.53 (3H, m), 3.86 (3H, s), 3.79-3.99 (2H, m), 4.00-4.17 (1H, m), 4.37-4.52 (1H, m), 6.64 (1H, d, J=9Hz), 6.79 (1H, s), 6.98-7.09 (2H, m), 7.11-7.28 (3H, m), 7.43-7.64 (4H, m)

Example 22

[0336] To a solution of 4-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide (327 mg) and pyridine (80.3 mg) in dichloromethane (6 ml) was added dropwise 2-nitrobenzenesulfonyl chloride (150 mg) at ambient temperature and the mixture was stirred at ambient temperature for 5 hours. The resulting mixture was diluted with dichloromethane (10 ml) and the organic layer was washed successively with saturated sodium bicarbonate aqueous solution and brine. Drying, filtering and removal of solvents afforded a crude product. The crude product was chromatographed on silica gel (eluent; 2-4% methanol in chloroform) to give 4-(2-nitrobenzenesulfonyl)-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (460 mg) .

NMR ($CDCl_3$, δ) : 1.47-1.82 (6H, m), 2.28 (3H, s), 2.31 (3H, s), 2.35-2.42 (6H, m), 3.30 (3H, s), 3.46-3.53 (5H, m), 3.60-3.68 (4H, m), 6.56-6.96 (6H, m), 7.53-7.88 (4H, m)

Example 23

[0337] A solution of 4-[2-[2-[3-(phthalimido)prop-1-yl]oxy]phenyl]vinyl-3-methoxybenzoic acid (370 mg) in tetrahydrofuran (20 ml) was treated at ambient temperature with triethylamine (246 mg), N-methyl-4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]aniline (297 mg), and diphenyl phosphorochloridate (326 mg). The reaction mixture was stirred at 80°C for 18 hours. After concentration, the residue was dissolved in chloroform and washed with brine and dried over magnesium sulfate. The crude product was purified by silica gel column chromatography (SiO_2 30 g, 3% methanol in chloroform) to give 4-[2-[2-[(3-(phthalimido)prop-1-yl)oxy]phenyl]vinyl]-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (550 mg).

NMR ($CDCl_3$, δ) : 1.47-1.95 (8H, m), 2.18-2.44 (12H, m), 3.31 and 3.34 (total 3H, s), 3.42-3.52 (2H, m), 3.57-3.72 (5H, m), 3.82-4.16 (6H, m), 6.30-7.80 (16H, m)

Example 24

[0338] The following compounds were obtained according to a similar manner to that of Example 23.

1) 4-[N-Methyl-2-[(3-tert-butoxycarbonylaminoprop-1-yl)-oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.40-1.75 (8H, m), 1.44 (9H, s), 1.89-1.97 (2H, m), 2.29 (6H, s), 2.32-2.42 (6H, m), 3.24 (6H, s), 3.26-3.34 (2H, m), 3.44-3.67 (6H, m), 3.77-3.88 (3H, m), 6.48-6.82 (9H, m), 6.90-6.96 (1H, m), 7.06-7.13 (1H, m)
ESI-MASS (m/z) : 774 (M+H)

2) 4-[2-[(3-tert-Eutoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-(4-benzyloxyphenyl) benzamide
NMR ($CDCl_3$, δ) : 1.42 (9H, s), 2.09-2.20 (2H, m), 3.28-3.37 (2H, m), 3.48 (3H, s), 3.81 (3H, s), 4.22-4.33 (2H, m), 4.70-4.78 (1H, br), 5.00 (2H, s), 6.82-6.88 (3H, m), 6.97-7.13 (6H, m), 7.31-7.48 (6H, m), 8.23 (1H, d, J=8Hz), 8.44 (1H, d, J=8Hz)
ESI-MASS (m/z) : 640 (M+H)

3) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-benzyloxy-N-methyl-N-cyclohexylbenzamide
NMR ($CDCl_3$, δ) : 1.01-1.12 (2H, br), 1.40 (9H, s), 1.45-1.82 (10H, m), 2.81-3.07 (5H, m), 3.80-3.89 (2H, m), 4.40-4.49 (1H, m), 5.18 (2H, s), 6.94 (1H, d, J=8Hz), 7.02 (1H, d, J=8Hz), 7.07-7.15 (2H, m), 7.35-7.48 (6H, m), 8.27 (1H, d, J=8Hz) 8.68 (1H, d, J=8Hz)
ESI-MASS (m/z) : 616 (M+H)

4) 4-[(2-Benzyloxy)benzoyl]amino-3-chloro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.45 (2H, m), 1.45-1.57 (2H, m), 1.62-1.93 (6H, m), 2.22-2.40 (12H, m), 2.50-2.63 (1H, m), 2.95-3.08 (1H, m), 3.31 (3H, s), 3.80-4.00 (4H, m), 4.58-4.70 (1H, m), 5.37 (2H, s), 6.56-6.62 (2H, m), 6.83-6.88 (1H, m), 7.02-7.13 (3H, m), 7.36-7.47 (7H, m), 8.27 (1H, d, J=7Hz), 8.42 (1H, d, J=7Hz)

5) 4-[N-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]phenyl]-tert-butoxycarbonylamino]methyl-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30 and 1.33 (total 9H, s), 1.43 (9H, s), 1.49-1.60 (2H, m), 1.62-1.98 (6H, m), 2.28 (3H, s), 2.30 (3H, s), 2.32-2.42 (6H, m), 3.20-3.29 (2H, m), 3.32 (3H, s), 3.39 (1H, s), 3.46-3.55 (4H, m), 3.62 (2H, br), 3.82 (1H, br), 3.88-4.03 (3H, m), 6.50-6.60 (2H, m), 6.65-7.00 (6H, m), 7.06-7.22 (2H, m)

6) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]phenoxy]-methyl-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.37 (9H, s), 1.47-1.57 (2H, m), 1.66-1.73 (2H, m), 1.73-1.88 (2H, m), 1.93-2.02 (2H, m), 2.28 (3H, s), 2.30 (3H, s), 2.32-2.40 (6H, m), 3.32 (3H, m), 3.25-3.38 (2H, m), 3.47-3.50 (2H, m), 3.62-3.67 (2H, m), 3.70 (3H, s), 3.80-3.88 (1H, m), 3.90-3.98 (2H, m), 4.07-4.17 (2H, m), 5.10 (2H, s), 5.50 (1H, br), 6.53-6.60 (2H, m), 6.70-6.90 (7H, m), 7.15-7.20 (1H, m)

7) 3-Benzyloxy-4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonyipent-1-yloxy]-4-methylphenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.85 (10H, m), 2.28 (3H, s), 2.29 (3H, s), 2.32-2.39 (6H, m), 2.90-2.98 (2H, m), 3.30 (3H, s), 3.47-3.49 (2H, m), 3.60-3.63 (2H, m), 3.77-3.98 (4H, m), 4.97 (2H, s), 6.56-6.60 (2H, m), 6.80 (1H, d, J=7Hz), 6.89-6.97 (2H, m), 7.04-7.12 (2H, m), 7.33-7.45 (6H, m), 8.19 (1H, d, J=6Hz), 8.41 (1H, d, J=7Hz)

8) 2-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-l-yloxy]-4-methylphenyl]-5-thiophenecarboxamide
NMR ($CDCl_3$, δ) : 1.37 (9H, s), 1.48-1.62 (2H, m), 1.62-1.76 (6H, m), 1.97-2.11 (2H, m), 2.17-2.38 (9H, m), 2.39 (3H, s), 3.31 (3H, s), 3.33-3.65 (6H, m), 3.87 (1H, br), 3.94 (1H, br), 4.02 (1H, s), 4.13-4.20 (2H, m), 6.40-6.57 (2H, m), 6.74-6.82 (2H, m), 6.92-7.14 (3H, m), 7.40-7.52 (1H, m), 8.10-8.27 (1H, m)

Example 25

[0339] A solution of (S)-4-[2-[1-methyl-3-(phthalimido)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (1.1 g) in methanol (30 ml) was stirred and treated with 40% methylamine in methanol (10 ml). The reaction mixture was refluxed for 30 minutes. Then the solvent was concentrated and purified by silica gel column chromatography (SiO_2 40 g, chloroform/methanol/ammonia = 90/10/0.5) to give (S)-4-[2-[(3-amino-1-methylprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yloxy]phenyl]benzamide.

NMR ($CDCl_3$, δ) : 1.42 (3H, d, J=7Hz), 1.46-1.92 (9H, m), 1.98-2.16 (1H, m), 2.20-2.45 (12H, m), 2.86 (2H, t, J=7Hz), 3.32 (3H, s), 3.42-3.53 (2H, m), 3.57-3.67 (2H, m), 3.79 (3H, s), 3.82-4.03 (2H, m), 4.73-4.90 (1H, m), 6.51-6.68 (2H, m), 6.79-6.95 (2H, m), 6.98-7.12 (3H, m), 7.37-7.49 (1H, m), 8.21 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

Example 26

[0340] A solution of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-(5-carboxypent-1-yloxy)-4-methylphenyl]benzamide (3.5 g) in ethyl acetate (30 ml) was treated at ambient temperature with triethylamine (575 mg), N-methylpiperazine (569 mg), and diphenylphosphoryl azide (1.56 g). The reaction mixture was stirred at the same temperature for 17 hours. The reaction mixture was washed with brine and dried over magnesium sulfate. The crude product was purified by silica gel column chromatography (SiO_2 100 g, 3% methanol in chloroform) to give 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (2.93 g).

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.42-1.60 (2H, m), 1.62-1.90 (4H, m), 2.06-2.20 (2H, m), 2.22-2.42 (12H, m), 3.21-3.36 (5H, m), 3.42-3.51 (2H, m), 3.56-3.67 (2H, m), 3.77 (3H, s), 3.81-4.02 (2H, m), 4.23 (2H, t, J=7Hz), 4.86 (1H, m), 6.51-6.67 (2H, m), 6.79-6.93 (2H, m), 6.94-7.13 (3H, m), 7.44 (1H, m), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

Example 27

[0341] The following compound was obtained according to a similar manner to that of Example 26.

4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.46-1.95 (8H, m), 2.06-2.42 (16H, m), 2.56 (1H, m), 3.00 (1H, m), 3.22-3.38 (5H, m), 3.79 (3H, s), 3.83-4.03 (3H, m), 4.25 (2H, t, J=7Hz), 4.61 (1H, m), 4.87 (1H, m), 6.52-6.68 (2H, m), 6.79-6.95 (2H, m), 6.96-7.17 (3H, m), 7.46 (1H, m), 8.21 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

Example 28

[0342] To a solution of 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-carboxypent-1-yl)oxy-4-methylphenyl]benzamide (300 mg) and N-methylmorpholine (45 mg), in N,N-dimethylformamide (5 ml) was added isobutyl chloroformate (61 mg) at -15°C and the solution was stirred at the same temperature for 5 minutes. N,N,N'-Trimethylethylenediamine (54 mg) was added to the solution and the mixture was stirred at -15°C for 30 minutes, and then at ambient: temperature for 1 hour. The mixture was diluted with ethyl acetate (20 ml) and the solution was washed successively with aqueous sodium hydrogen carbonate solution, water (15 ml x 3) and brine. The solution was dried over potassium carbonate and the solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography (SiO_2 40 g, 1-5% methanol in chloroform) to give 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[(2-dimethylaminoeth-1-yl)-N-methylaminocarbonyl]pent-1-yl]oxy-4-methylphenyl]benzamide (312 mg).

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.44-2.21 (8H, m), 2.25 (3H, s), 2.27 (6H, s), 2.29-2.50 (4H, m), 2.91 (1H, s), 3.00 (2H, s), 3.26-3.51 (4H, m), 3.31 (3H, s), 3.77 (3H, s), 3.81-4.02 (2H, m), 4.22 (2H, t, J=5Hz), 4.88 (1H, br), 6.52-6.68 (2H, m), 6.79-7.11 (5H, m), 7.43 (1H, m), 8.20 (1H, d, J=9Hz), 8.40 (1H, d, J=8Hz)

Example 29

[0343] The following compounds were obtained according to a similar manner to that of Example 28.

1) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(3-dimethylaminoprop-1-yl)aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.42-1.57 (2H, m), 1.61-1.85 (6H, m), 2.04-2.35 (8H, m), 2.25 (3H, s), 2.29 (9H, s), 2.46 (2H, t, J=6Hz), 3.20-3.38 (4H, m), 3.30 (3H, s), 3.76 (3H, s), 3.80-4.00 (2H, m), 4.24 (2H, t, J=5Hz), 4.90 (1H,

br), 6.61-6.72 (2H, m), 6.84-7.12 (6H, m), 7.43 (1H, d, J=8Hz), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

2) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-oxopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.50-1.92 (8H, m), 2.15 (2H, t, J=6Hz), 2.29 (2H, t, J=5Hz), 2.38-2.51 (6H, m), 3.30 (2H, t, J=5Hz), 3.32 (3H, s), 3.70-4.05 (6H, m), 3.80 (3H, s), 4.25 (2H, t, J=5Hz), 4.85 (1H, br), 6.55-6.67 (2H, m), 6.83-7.15 (6H, m), 7.40-7.51 (1H, m), 8.20 (1H, d, J=8Hz), 8.40 (1H, br)

3) 4-[2-(3-tert-Butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-pyridylaminocarbonyl)pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.50-1.61 (2H, m), 1.75-1.93 (4H, m), 2.09-2.20 (2H, m), 2.30 (3H, s), 2.42 (2H, br), 3.30 (1H, q, J=5Hz), 3.36 (3H, s), 3.70 (3H, s), 3.72-4.00 (2H, m), 4.25 (2H, t, J=5Hz), 4.90 (1H, br), 6.60 (1H, br), 6.72 (1H, d, J=8Hz), 6.99-7.12 (6H, m), 7.43-7.51 (1H, m), 7.63 (1H, d, J=8Hz), 8.19 (1H, d, J=8Hz), 8.42 (1H, d, J=7Hz), 8.46 (1H, br), 9.22 (1H, br)

Example 30

[0344] To a solution of 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-carboxypent-1-yl)oxy-4-methylphenyl]benzamide (250 mg) and N-methylmorpholine (37 mg) in dichloromethane (5 ml) was added pivaloyl chloride (45 mg) at -15°C. After being stirred at the same temperature for 5 minutes, to the mixture was added 1-amino-4-methylpiperazine (47 mg) and the mixture was stirred at -15°C for 1 hour and then stirred at ambient temperature for additional 2 hours. The resulting mixture was poured into saturated aqueous sodium hydrogen carbonate solution (20 ml) and the solution was extracted with chloroform (15 ml x 3). The organic layer was washed with brine and dried over magnesium sulfate. The solvent was evaporated and the residue was purified on silica gel column chromatography (SiO_2 30 g, 1-15% methanol in chloroform) to give 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide (208 mg) .

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.90 (6H, m), 2.10-2.19 (2H, m), 2.24 (3H, s), 2.25 (3H, s), 2.51 (2H, t, J=5Hz), 2.54-2.91 (8H, m), 3.30 (2H, t, J=5Hz), 3.34 (3H, s), 3.75 (3H, s), 3.80-4.03 (2H, m), 4.24 (2H, t, J=5Hz), 4.78-4.97 (1H, br), 6.53-6.67 (2H, m), 6.73-7.14 (6H, m), 7.40-7.50 (1H, m), 8.21 (1H, d, J=8Hz), 8.45 (1H, d, J=8Hz)

Example 31

[0345] The following compounds were obtained according to a similar manner to that of Example 9.

1) 4-[2-(E)-[2-(4-Methylpiperazin-1-yl)carbonylethen-1-yl]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 1.48-1.59 (2H, m), 1.67-1.76 (2H, m), 1.79-1.87 (2H, m), 2.21 (3H, s), 2.26 (3H, s), 2.31 (3H, s), 2.31-2.44 (10H, m), 3.17-3.25 (2H, m), 3.34 (3H, s), 3.47-3.52 (2H, m), 3.56-3.67 (3H, m), 3.62 (3H, s), 3.82-3.99 (3H, m), 5.71 (1H, m), 6.60-6.67 (2H, m), 6.86 (1H, d, J=7Hz), 6.92 (1H, d, J=7Hz), 6.98-7.03 (2H, m), 7.14 (1H, d, J=7Hz), 7.43-7.62 (4H, m), 7.85 (1H, d, J=7Hz)

2) 4-[2-[(4-Methylpiperazin-1-yl)carbonylmethoxy]benzoyl]-amino-3-methoxy-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.30-1.90 (6H, m), 2.14 (3H, s), 2.26 (3H, s), 2.35-2.46 (3H, m), 3.34 (3H, s), 3.46-3.55 (4H, m), 3.59-3.68 (4H, m), 3.72 (3H, s), 3.80-4.01 (2H, m), 4.90 (2H, s), 6.58-6.68 (2H, m), 6.82-7.06 (4H, m), 7.13-7.20 (2H, m), 7.46-7.51 (1H, m), 8.19 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

Example 32

[0346] A solution of 4-(2-iodobenzoyl)amino-N-[2-(4-methoxyphenyl)methoxy]phenyl-N-methylbenzamide (2.30 g) in a mixture of dichloromethane (30 ml) and trifluoroacetic acid (15 ml) was stirred at ambient temperature for 2 hours and the solvent was evaporated in vacuo. The residual oil was dissolved in chloroform (50 ml) and the solution was washed successively with water (50 ml), aqueous sodium hydrogen carbonate (50 ml) and brine (25 ml). The solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give 4-(2-iodobenzoyl)amino-N-(2-hydroxy)phenyl-N-methylbenzamide (1.20 g) .

NMR (DMSO-d_6, δ) : 3.20 (3H, s), 6.69 (1H, t, J=7Hz), 6.82 (1H, d, J=7Hz), 6.98-7.05 (3H, m), 7.40-7.54 (4H, m), 7.90 (1H, d, J=7Hz), 9.84 (1H, s)

Example 33

[0347] The following compounds were obtained according to a similar manner to that of Example 32.

1) 4-(2-Hydroxybenzoyl)amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]-phenylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 2.32 (3H, s), 2.35-2.51 (4H, m), 3.36 (3H, s), 3.59-3.89 (2H, m), 5.02 (2H, s), 6.63-6.72 (2H, m), 6.88 (1H, t, J=7Hz), 7.00 (2H, d, J=8Hz), 7.20-7.46 (9H, m), 7.70 (1H, d, J=7Hz), 8.68 (1H, s)

2) 3-Methoxy-4-(2-hydroxybenzoyl)amino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]-phenylmethoxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 2.23 (3H, s), 2.30 (3H, s), 2.33-2.51 (4H, m), 3.37 (3H, s), 3.41-3.56 (2H, m), 3.68 (3H, s), 3.72-3.87 (2H, m), 4.91 (1H, d, J=14Hz), 5.09 (1H, d, J=14Hz), 6.63-6.71 (2H, m), 6.35-6.93 (2H, m), 7.00 (2H, d, J=8Hz), 7.33-7.50 (7H, m), 8.14 (1H, d, J=7Hz), 8.72 (1H, s)

3) 4[2-(3-Hydroxyprop-1-yl)thiobenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.58 (2H, m), 1.61-1.73 (2H, m), 1.77-1.89 (2H, m), 2.28 (3H, s), 2.31-2.40 (6H, m), 3.02 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.42-3.50 (2H, m), 3.56-3.65 (2H, m), 3.67-3.78 (7H, m), 3.81-4.01 (2H, m), 6.58-6.67 (2H, m), 6.81-6.95 (2H, m), 7.03 (1H, s), 7.25 (1H, m), 7.36-7.50 (2H, m), 7.64 (1H, d, J=7Hz), 8.30 (1H, d, J=7Hz), 8.77 (1H, s)

Example 34

[0348] The following compound was obtained by using 2-nitro-4-(2-benzyloxybenzoyl)amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide as a starting compound according to a similar manner to that of Example 10.

2-Amino-4-(2-hydroxybenzoyl)amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.21-2.02 (10H, m), 2.28-2.44 (12H, m), 2.48-2.69 (1H, m), 2.93-3.08 (1H, m), 3.30 (3H, s), 3.80-4.06 (4H, m), 4.68 (1H, br), 4.73 (2H, s), 5.32 (1H, s), 6.53-6.62 (3H, m), 6.78-6.96 (5H, m), 7.33-7.44 (1H, m), 7.78-7.88 (1H, m)

Example 35

[0349] A mixture of 4-(2-hydroxybenzoyl)amino-3-methoxy-N-(2-benzyloxy-4-methyl)phenyl-N-methylbenzamide (550 mg), 1-(tert-butoxycarbonyl)-4-hydroxypiperidine (223 mg), diethyl azodicarboxylate (193 mg) and triphenylphosphine (291 mg) in tetrahydrofuran (15 ml) was stirred at ambient temperature for 8 hours and the mixture was diluted with ethyl acetate (25 ml). The solution was washed with water and brine, and organic phase was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by silica gel column (30% ethyl acetate in n-hexane) to give 3-methoxy-4-[2-[1-(tert-butoxycarbonyl)piperidin-4-yl]oxybenzoyl]amino-N-(2-benzyloxy-4-methyl) phenyl-N-methylbenzamide (562 mg).

NMR ($CDCl_3$, δ) : 1.44 (9H, s), 1.72-1.90 (2H, m), 1.95-2.12 (2H, m), 2.27 (3H, s), 2.95-3.16 (4H, m), 3.37 (3H, s), 3.60 (3H, s), 3.73-4.00 (2H, m), 4.64 (1H, m), 4.88 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.65-6.71 (2H, m), 6.86 (1H, d, J=7Hz), 6.95-7.03 (3H, m), 7.09 (1H, t, J=7Hz), 7.25-7.50 (6H, m), 8.18 (1H, d, J=7Hz), 8.35 (1H, d, J=7Hz)

Example 36

[0350] The following compounds were obtained according to a similar manner to that of Example 35.

1) (S)-4-[2-[1-Methyl-3-(phthalimido)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43 (3H, d, J=7Hz), 1.47-1.92 (7H, m), 1.98-2.13 (1H, m), 2.20-2.47 (12H, m), 3.32 (3H, s), 3.42-3.53 (2H, m), 3.57-3.67 (2H, m), 3.73-4.05 (7H, m), 4.77 (1H, m), 6.51-6.69 (2H, m), 6.78-7.12 (5H, m), 7.42 (1H, m), 7.57 (4H, s), 8.08-8.24 (2H, m)

2) (R)-4-[2-[[4-[Phthalimido-1-yl)but-2-yl]oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide

NMR ($CDCl_3$, δ) : 1.44 and 1.47 (total 3H, s), 1.52-1.92 (8H, m), 2.02-2.12 (1H, m), 2.28 (3H, s), 2.30 (3H, s), 2.33-2.42 (6H, m), 3.35 (3H, s), 3.47-3.53 (2H, m), 3.60-3.67 (2H, m), 3.80 (3H, s), 3.85-4.00 (2H, br), 3.88 (2H, t, J=8Hz), 4.74-4.82 (1H, br), 6.57-6.69 (2H, m), 6.81-6.95 (2H, m), 6.98-7.09 (3H, m), 7.43 (1H, t, J=8Hz), 7.53-7.60 (4H, br), 8.14 (1H, d, J=8Hz), 8.20 (1H, d, J=8Hz)
ESI-MASS (m/z) : 804 (M+H)

3) (R)-4-[2-[[4-(Phthalimido-1-yl)but-2-yl]oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethyl-aminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.42 and 1.45 (total 3H, s), 1.50-1.90 (12H, m), 2.02-2.10 (1H, m), 2.28 (9H, s), 2.32-2.41 (4H, m), 2.52-2.62 (1H, m), 2.97-3.06 (1H, m), 3.35 (3H, s), 3.80 (3H, s), 3.87 (2H, t, J=8Hz), 3.90-3.97 (2H, m), 4.58-4.68 (1H, m), 4.72-4.81 (1H, m), 6.57-6.67 (2H, m), 6.81-6.93 (2H, m), 6.98-7.08 (3H, m), 7.43 (1H, t, J=8Hz), 7.53-7.59 (4H, br s), 8.13 (1H, d, J=8Hz), 8.20 (1H, d, J=8Hz)

4) (S)-4-[2-[[4-(Phthalimido-1-yl)but-2-yl]oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethyl-aminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide
NMR ($CDCl_3$, δ) : 1.42 and 1.44 (total 3H, s), 1.50-1.91 (12H, m), 2.02-2.10 (1H, m), 2.29 (9H, s), 2.32-2.41 (4H, m), 2.52-2.62 (1H, m), 2.95-3.05 (1H, m), 3.36 (3H, s), 3.80 (3H, s), 3.86 (2H, t, J=8Hz), 3.90-3.97 (2H, m), 4.58-4.66 (1H, m), 4.72-4.80 (1H, m), 6.57-6.67 (2H, m), 6.81-6.92 (2H, m), 6.98-7.08 (3H, m), 7.44 (1H, t, J=8Hz), 7.53-7.60 (4H, br s), 8.13 (1H, d, J=8Hz), 8.21 (1H, d, J=8Hz)
ESI-MASS (m/z) : 832 (M+1)

5) 3-Methoxy-4-[2-[3-(phthalimido)-1-methylprop-1-yl]oxybenzoyl]amino-N-(2-benzyloxy-4-methyl)phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.41 (3H, d, J=7.5Hz), 1.96-2.12 (2H, m), 2.24 (3H, s), 2.27-2.42 (2H, m), 3.39 (3H, s), 3.60-3.69 (2H, m), 3.86 (2H, t, J=7.5Hz), 4.77 (1H, m), 4.94 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.66-6.82 (3H, m), 6.95-7.08 (4H, m), 7.20-7.71 (10H, m), 8.10-8.21 (2H, m)

Example 37

[0351] The following compounds were obtained according to a similar manner to that of Example 14.

1) 4-[2-(3-Acetylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-(2-acetoxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.86 (3H, s), 2.10-2.19 (2H, m), 2.30 (3H, s), 3.41 (2H, q, J=5Hz), 3.72 (3H, s), 4.21 (2H, t, J=5Hz), 5.94 (1H, br), 6.85 (1H, s), 6.90-7.11 (6H, m), 7.42-7.49 (1H, m), 8.10 (1H, d, J=8Hz), 8.42 (1H, d, J=8Hz)

2) 4-[2-(3-Acetylamincprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl) carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.64 (2H, m), 1.58-1.85 (4H, m), 1.88 (3H, s), 2.12 (2H, t, J=5Hz), 2.29 (6H, s), 2.34-2.42 (2H, m), 2.57 (2H, t, J=5Hz), 3.30 (2H, q, J=5Hz), 3.32 (3H, s), 3.39 (2H, q, J=5Hz), 3.72-3.79 (2H, m), 3.76 (3H, s), 3.83-4.00 (2H, m), 4.20 (2H, t, J=5Hz), 6.33 (1H, br), 6.57-6.67 (2H, m), 6.83-7.10 (6H, m), 7.43 (1H, dd, J=2, 7Hz), 8.10 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

Example 38

[0352] To an ice bath cooled solution of 4-[2-(3-aminoprop-1-yl)oxybenzoyl]amino-N-[2-(5-carboxypent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide (650 mg) in dichloromethane (20 ml) were added triethylamine (137 mg) and di-tert-butyldicarbonate (296 mg) and the mixture was stirred at ambient temperature overnight. The solution was washed successively with water, 10% hydrochloric acid, saturated aqueous sodium hydrogen carbonate and brine, and the organic phase was dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-[2-[3-(tert-butoxy-carbonyl)-aminoprop-1-yl]oxybenzoyl]amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide (749 mg).

NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7.5Hz), 1.40 (9H, s), 1.44-1.56 (2H, m), 1.66-1.76 (2H, m), 1.76-1.87 (2H, m), 2.06-2.15 (2H, m), 2.28 (3H, s), 2.34 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.31-3.40 (2H, m), 3.85-3.97 (2H, m), 4.13 (2H, q, J=7.5Hz), 4.21 (2H, t, J=7.5Hz), 4.74 (1H, br), 6.54-6.62 (2H, m), 6.86 (1H, d, J=7Hz), 6.98 (1H, d, J=7Hz), 7.09 (1H, d, J=7Hz), 7.32 (2H, d, J=8Hz), 7.41-7.52 (3H, m), 8.11 (1H, d, J=7Hz), 9.87 (1H, s)

Example 39

[0353] The following compound was obtained according to a similar manner to that of Example 38.

3-Methoxy-4-[2-[3-(tert-butoycarbonyl)amino-1-methylprop-1-yl]oxybenzoyl]amino-N-(2-benzyloxy-4-methyl)-phenyl-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.37 (9H, s), 1.41 (3H, d, J=7.5Hz), 1.84-2.11 (2H, m), 2.28 (3H, s), 3.20-3.31 (2H, m), 3.40 (3H, s), 3.64 (3H, s), 4.61 (1H, br), 4.72 (1H, m), 4.90 (1H, d, J=14Hz), 5.09 (1H, d, J=14Hz), 6.62-6.70 (2H, m), 6.84 (1H, d, J=7Hz), 6.93-7.12 (4H, m), 7.28-7.72 (6H, m), 8.22 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

Example 40

[0354] A solution of aqueous 4M sulfuric acid (0.5 ml) and 3-(phthalimid-1-yl)propanal (189 mg) in tetrahydrofuran (10 ml) was slowly added to a solution of 4-(2-aminobenzoylamino)-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenylbenzamide (560 mg) in tetrahydrofuran (10 ml) followed by the portionwise addition of sodium borohydride (59.8 mg) at 0°C. The mixture was diluted with 1,4-dioxane (5 ml) and stirred for an additional 1.5 hours at ambient temperature. The mixture was quenched with water (0.5 ml) and concentrated. The residue was partitioned with ethyl acetate and saturated aqueous sodium hydrogen carbonate. The organic extract was washed with brine and dried over sodium sulfate, concentrated, and purified by silica gel column chromatography (SiO_2, 30 g, 3% methanol in chloroform) to give 3-methoxy-4-[2-[3-(phthalimido)prop-1-yl]amino]benzoylamino-N-methyl-N-[2-[5-(4-methylpiperazin-l-yl)carbonylpent-l-yloxy]phenyl]benzamide (200 mg).

NMR ($CDCl_3$, δ) : 1.44-1.62 (2H, m), 1.63-1.93 (4H, m), 1.97-2.12 (2H, m), 2.21-2.46 (12H, m), 3.17-3.38 (5H, m), 3.42-3.56 (2H, m), 3.57-3.69 (2H, m), 3.70-4.04 (7H, m), 6.51-6.73 (4H, m), 6.78-6.96 (2H, m), 7.00 (1H, s), 7.20-7.35 (1H, m), 7.40 (1H, d, J=8Hz), 7.53-7.67 (3H, m), 7.72-7.86 (2H, m), 8.13 (1H, d, J=8Hz), 8.34 (1H, s)

Example 41

[0355] A solution of 4-(2-nitrobenzoyl)amino-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]-N-methylbenzamide (800 mg), 20% palladium hydroxide (200 mg) in ethanol (20 ml) was stirred under atmospheric pressure of hydrogen at ambient temperature. After 2 hours, the reaction mixture was filtered through a bed of Celite, and the solvent was removed by rotary evaporation and the crude product was purified by silica gel column chromatography (SiO_2 30 g, ethyl acetate/hexane = 3/1) to give 4-(2-aminobenzoyl)amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]-benzamide (700 mg).

NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7Hz), 1.41-1.57 (2H, m), 1.63-1.87 (4H, m), 2.27 (3H, s), 2.33 (2H, t, J=7Hz), 3.32 (3H, s), 3.78-4.00 (2H, m), 4.12 (2H, q, J=7Hz), 5.38-5.56 (2H, m), 6.55-6.64 (2H, m), 6.64-6.76 (2H, m), 6.87 (1H, d, J=9Hz), 7.22 (1H, d, J=9Hz), 7.28-7.50 (5H, m), 7.79 (1H, br s)

Example 42

[0356] The following compound was obtained according to a similar manner to that of Preparation 4.

4-(2-Aminobenzenesulfonyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide

NMR ($CDCl_3$, δ) : 1.45-1.54 (2H, m), 1.65-1.82 (4H, m), 2.30 (3H, s), 2.33 (3H, s), 2.35-2.43 (6H, m), 3.29 (3H, s), 3.46-3.51 (5H, m), 3.60-3.65 (4H, m), 4.84-4.89 (2H, m), 6.56-6.89 (6H, m), 7.28-7.48 (4H, m)

ESI-MASS (m/z) : 638 (M+H)

Example 43

[0357] A solution of 4-[2-(acetyloxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (400 mg) in methanol (10 ml) was treated with 1N sodium hydroxide solution (3 ml) at ambient temperature. After 6 hours, the reaction mixture was concentrated in vacuo and extracted with the mixture of dichloromethane and diluted hydrochloric acid. The organic phase was washed with brine and dried over sodium sulfate. The crude product was purified by silica gel column chromatography (SiO_2 30 g, 5% methanol in chloroform) to give 4-[2-(hydroxy)benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (290 mg).

NMR ($CDCl_3$, δ) : 1.27-2.00 (10H, m), 2.21-2.46 (12H, m), 2.56 (1H, m), 3.00 (1H, m), 3.33 (3H, s), 3.80 (3H, s), 3.82-4.05 (4H, m), 4.63 (1H, m), 6.55-6.68 (2H, m), 6.82-7.09 (5H, m), 7.42 (1H, m), 7.55 (1H, m), 8.20 (1H, m)

Example 44

[0358] The following compounds were obtained according to a similar manner to that of Example 43.

1) 4-(2-Hydroxybenzoyl)amino-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yloxy)-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.42-1.58 (2H, m), 1.61-1.90 (4H, m), 2.28 (3H, s), 2.33 (2H, t, J=7Hz), 3.32 (3H, s), 3.80 (3H, s), 3.81-4.02 (2H, m), 4.12 (2H, q, J=7Hz), 6.53-6.67 (2H, m), 6.80-6.98 (3H, m), 7.01 (1H, d, J=8Hz), 7.07 (1H, s), 7.42 (1H, dd, J=8, 8Hz), 7.49 (1H, d, J=8Hz), 8.18 (1H, d, J=8Hz), 8.72 (1H, s)

2) 4- (2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N- (2-methylphenyl)benzamide
NMR ($CDCl_3$, δ) : 2.21 (3H, s), 3.40 (3H, s), 3.78 (3H, s), 6.82-7.23 (9H, m), 7.37-7.53 (2H, m), 8.18 (1H, d, J=8Hz), 8.69 (1H, br s)

3) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.42-1.59 (2H, m), 1.60-1.89 (4H, m), 2.20-2.46 (12H, m), 3.32 (3H, s), 3.42-3.53 (2H, m), 3.57-3.69 (2H, m), 3.71-4.02 (6H, m), 6.51-6.68 (2H, m), 6.79-7.08 (5H, m), 7.40 (1H, m), 7.51 (1H, d, J=8Hz), 8.18 (1H, d, J=8Hz), 8.86 (1H, br s)

4) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-(2-benzyloxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.30 (3H, s), 3.38 (3H, s), 3.63 (3H, s), 4.89 (1H, d, J=13Hz), 5.08 (1H, d, J=13Hz), 6.62-6.68 (2H, m), 6.82-7.00 (6H, m), 7.28-7.42 (5H, m), 7.47 (1H, d, J=8Hz), 8.13 (1H, d, J=8Hz), 8.79 (1H, s)

5) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-[2-[4-(2-oxazolin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.28 (3H, s), 3.40 (3H, s), 3.67 (3H, s), 4.06 (2H, t, J=10Hz), 4.41 (2H, t, J=10Hz), 4.92 (1H, d, J=12Hz), 5.10 (1H, d, J=12Hz), 6.60 (1H, s), 6.71 (1H, d, J=8Hz), 6.87-7.08 (5H, m), 7.28 (1H, d, J=8Hz), 7.42 (1H, dd, J=2, 8Hz), 7.52 (1H, d, J=8Hz), 8.16 (1H, d, J=8Hz), 8.82 (1H, s)

6) 4-(2-Hydroxybenzoyl)amino-3-methyl-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48 (2H, br), 1.60-1.81 (4H, m), 2.19 (3H, s), 2.28 (3H, s), 2.30-2.35 (3H, m), 2.38 (3H, s), 2.50 (4H, br), 3.30 (3H, s), 3.52 (2H, br), 3.69 (2H, br), 3.83 (1H, br), 3.92 (1H, br), 6.62 (2H, s), 6.89-6.93 (2H, m), 7.02-7.10 (2H, m), 7.35 (1H, s), 7.40-7.47 (1H, m), 7.63-7.70 (2H, m), 8.52 (1H, br)

Example 45

[0359] A solution of 4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (542 mg) in 90% trifluoroacetic acid (10 ml) was stirred at ambient temperature for 3 hours and the solvent was evaporated in vacuo. The residue was stirred with chloroform (20 ml) and saturated aqueous sodium hydrogen carbonate (10 ml) and the organic phase was separated. The solution was washed with brine and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-[2-(3-aminoprop-1-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy] phenylbenzamide (465 mg) .

NMR ($CDCl_3$, δ) : 1.47-1.59 (2H, m), 1.67-2.00 (6H, m), 2.06-2.66 (2H, m), 2.35 (3H, s), 2.39 (3H, s), 2.32-2.41 (4H, m), 2.96 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.45-3.50 (2H, m), 3.58-3.65 (2H, m), 3.89-3.99 (2H, m), 4.29 (2H, d, J=7.5Hz), 6.54-6.62 (2H, m), 6.85 (1H, d, J=7Hz), 7.01 (1H, d, J=7Hz), 7.10 (1H, t, J=7Hz), 7.32 (2H, d, J=8Hz), 7.43-7.50 (3H, m), 8.20 (1H, d, J=7Hz)

Example 46

[0360] The following compounds were obtained according to a similar manner to that of Example 45.

1) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40-1.92 (6H, m), 1.98-2.12 (2H, m), 2.19-2.44 (12H, m), 2.90 (2H, t, J=7Hz), 3.32 (3H, s), 3.40-3.53 (2H, m), 3.56-3.68 (2H, m), 3.78 (3H, s), 3.80-4.02 (2H, m), 4.28 (2H, t, J=7Hz), 6.51-6.67 (2H, m), 6.78-6.95 (2H, m), 6.97-7.16 (3H, m), 7.44 (1H, m), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

2) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.26-1.92 (12H, m), 1.98-2.12 (2H, m), 2.27 (9H, s), 2.29-2.42 (3H, m), 2.56 (1H, m), 2.89 (2H, t, J=7Hz), 3.00 (1H, m), 3.32 (3H, s), 3.78 (3H, s), 3.82-4.02 (3H, m), 4.27 (2H, t, J=7Hz), 4.61 (1H, m), 6.52-6.67 (2H, m), 6.79-6.96 (2H, m), 6.97-7.12 (3H, m), 7.43 (1H, m), 8.21 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

3) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperidin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 0.95 (3H, d, J=7.5Hz), 1.00-1.14 (2H, m), 1.46-1.90 (8H, m), 2.01-2.12 (2H, m), 2.26 (3H, s), 2.34 (2H, t, J=7.5Hz), 2.52 (1H, m), 2.85-3.03 (3H, m), 3.31 (3H, s), 3.79 (3H, s), 3.79-4.00 (4H, m), 4.32 (2H, t, J=7.5Hz), 4.55 (1H, m), 6.58 (1H, d, J=7Hz), 6.62 (1H, s), 6.84 (1H, d, J=7Hz), 6.90 (1H, d, J=7Hz), 7.00-7.11 (3H, m), 7.42 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

4) 4- [2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N- [2-[5-[(2S)-carbamoylpyrrolidin-1-yl]carbonylpent-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.48-2.20 (12H, m), 2.28 (3H, s), 2.32-2.40 (2H, m), 2.88-3.00 (2H, m), 3.31 (3H, s), 3.33-3.61 (2H, m), 3.80 (3H, s), 3.82-3.99 (2H, m), 4.29 (2H, t, J=7Hz), 4.54 (1H, m), 6.52-6.63 (2H, m), 6.81-7.10 (5H, m), 7.43 (1H, t, J=7Hz), 8.14 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

5) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-aminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.63-1.94 (4H, m), 1.99-2.18 (2H, m), 2.23 (3H, s), 2.62-3.07 (2H, m), 3.29 (3H, s), 3.29-3.51 (2H, m), 3.75-4.00 (2H, m), 3.76 (3H, s), 4.21 (2H, t, J=7.5Hz), 6.56-6.85 (4H, m), 7.28-7.62 (2H, m), 8.13 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

6) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-acetylaminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.60-1.86 (4H, m), 2.00 (3H, s), 2.08-2.20 (2H, m), 2.27 (3H, s), 2.93-3.03 (2H, m), 3.30 (3H, s), 3.30-3.50 (2H, m), 3.77 (3H, s), 3.83-3.98 (2H, m), 4.26 (2H, t, J=7.5Hz), 6.53-6.65 (2H, m), 6.86-7.12 (5H, m), 7.42 (1H, t, J=7Hz), 8.12 (1H, d, J=7Hz), 8.37 (1H, d, J=7Hz)

7) 3-Methoxy-4-[2-(piperidin-4-yl)oxybenzoyl]amino-N-(2-hydroxy-4-methyl)phenyl-N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.50-1.62 (2H, m), 1.94-2.05 (2H, m), 2.14 (3H, s), 2.57 (2H, t, J=7.5Hz), 2.91-3.00 (2H, m), 3.16 (3H, s), 3.75 (3H, s), 4.73 (1H, m), 6.48 (1H, d, J=7Hz), 6.64 (1H, s), 7.87 (1H, d, J=7Hz), 7.92 (1H, d, J=7Hz), 7.01 (1H, s), 7.09 (1H, t, J=7Hz), 7.32 (1H, d, J=7Hz), 7.52 (1H, t, J=7Hz), 8.02 (1H, d, J=7Hz), 8.27 (1H, d, J=7Hz)

8) 3-Methoxy-4-[2-(piperidin-4-yl)oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.46-1.88 (8H, m), 2.07-2.19 (2H, m), 2.26 (3H, s), 2.29 (3H, s), 2.32-2.41 (6H, m), 2.72 (2H, t, J=7.5Hz), 3.10-3.20 (2H, m), 3.32 (3H, s), 3.45-3.50 (2H, m), 3.60-3.66 (2H, m), 3.80 (3H, s), 3.83-4.00 (2H, m), 4.57 (1H, m), 6.58 (1H, d, J=7Hz), 6.62 (1H, s), 6.82-6.91 (2H, m), 6.98-7.11 (3H, m), 7.43 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

9) 4-[2-(3-Amino-1-methylprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.42 (3H, d, J=7.5Hz), 1.46-1.89 (6H, m), 1.99-2.11 (2H, m), 2.28 (3H, s), 2.30 (3H, s), 2.31-2.42 (6H, m), 2.85 (2H, t, J=7.5Hz), 3.33 (3H, s), 3.45-3.50 (2H, m), 3.59-3.66 (2H, m), 3.80 (3H, s), 3.84-4.01 (2H, m), 4.80 (1H, m), 6.59 (1H, d, J=7Hz), 6.63 (1H, s), 6.82-6.92 (2H, m), 7.01-7.10 (3H, m), 7.44 (1H, t, J=7Hz), 8.22 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

10) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-aminocarbonylpent-1-yl)oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40-1.59 (2H, m), 1.61-1.90 (4H, m), 2.11-2.30 (4H, m), 2.35 (3H, s), 3.00 (2H, t, J=6Hz), 3.11 (2H, br), 3.29 (3H, s), 3.75 (3H, s), 3.76-4.02 (2H, m), 4.23 (2H, t, J=5Hz), 6.00 (1H, br), 6.50 (1H, br), 6.55-6.71 (2H, m), 6.87-7.12 (5H, m), 7.42 (1H, dd, J=2, 7Hz), 8.10 (1H, d, J=9Hz), 8.36 (1H, d, J=8Hz)

11) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(morpholin-4-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.48-1.90 (6H, m), 2.11 (2H, t, J=5Hz), 2.26 (3H, s), 2.21-2.52 (6H, m), 2.79-2.90 (3H, m), 2.96 (2H, t, J=5Hz), 3.31 (3H, s), 3.40-3.49 (2H, m), 3.52-3.62 (2H, m), 3.80 (3H, s), 3.83-4.04 (2H, m), 4.29 (2H, t, J=5Hz), 6.57-6.68 (2H, m), 6.81-7.12 (6H, m), 7.41-7.50 (1H, m), 8.17 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

12) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-oxopiperidin-1-yl)carbonylpent-1-yl]oxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-2.05 (8H, m), 2.11 (2H, t, J=5Hz), 2.28 (3H, s), 2.41-2.52 (2H, m), 2.96 (2H, t, J=5Hz), 3.31 (3H, s), 3.70-4.61 (8H, m), 6.52-7.55 (8H, m), 8.02-8.46 (3H, m)

13) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-(2-methoxy-4-methylphenyl)-N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.90-1.98 (2H, m), 2.25 (3H, s), 2.71 (2H, t, J=6Hz), 3.19 (3H, s), 3.73 (3H, s), 4.32 (2H, t, J=5Hz), 6.67 (1H, d, J=8Hz), 6.80-6.96 (2H, m), 7.26 (1H, d, J=8Hz), 7.55 (1H, dd, J=2,8Hz), 8.03 (1H, d, J=8Hz), 8.29 (1H, d, J=8Hz)

14) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(thiazol-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.02-2.10 (2H, m), 2.29 (3H, s), 2.89 (2H, t, J=5Hz), 3.40 (3H, s), 3.64 (3H, s), 4.25 (2H, t, J=5Hz), 4.90 (1H, d, J=11Hz), 5.09 (1H, d, J=11Hz), 6.62-6.71 (2H, m), 6.88 (1H, d, J=8Hz), 6.98-7.10 (5H, m), 7.24-7.48 (4H, m), 7.81 (1H, d, J=3Hz), 7.95 (1H, d, J=8Hz), 8.20 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz)

15) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(oxazol-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.00-2.11 (2H, m), 2.29 (3H, s), 2.89 (2H, t, J=5Hz), 3.40 (3H, s), 3.66 (3H, s), 4.91 (1H, d, J=12Hz), 5.10 (1H, d, J=12Hz), 6.64 (1H, s), 6.70 (1H, d, J=8Hz), 6.87 (1H, d, J=8Hz), 7.00-7.12 (4H, m), 7.21 (1H, s), 7.25-7.49 (4H, m), 7.65 (1H, s), 8.04 (1H, d, J=8Hz), 8.23 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz)

16) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(2-oxazolin-2-yl)phenylmethyl]oxymethylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.02-2.11 (2H, m), 2.28 (3H, s), 2.90 (2H, t, J=5Hz), 3.39 (3H, s), 3.67 (3H, s), 4.05 (2H, t, J=9Hz), 4.29 (2H, t, J=5Hz), 4.41 (2H, t, J=5Hz), 4.89 (1H, d, J=12Hz), 5.09 (1H, d, J=12Hz), 6.63 (1H, s), 6.70 (1H, d, J=8Hz), 6.84 (1H, d, J=8Hz), 7.00-7.12 (4H, m), 7.37 (2H, d, J=8Hz), 7.41 (1H, d, J=8Hz), 7.93 (2H, d, J=5Hz), 8.20 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

17) 4-[2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N- [2-[4-(pyrimidin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.05-2.14 (2H, m), 2.27 (3H, s), 2.89 (2H, t, J=5Hz), 3.38 (3H, s), 3.64 (3H, s), 4.24 (2H, t, J=5Hz), 4.94 (1H, d, J=13Hz), 5.12 (1H, d, J=13Hz), 6.65-6.72 (2H, m), 6.85 (1H, d, J=8Hz), 6.97-7.18 (5H, m), 7.39-7.46 (3H, m), 8.13 (1H, d, J=8Hz), 8.35 (1H, d, J=8Hz), 8.41 (2H, d, J=8Hz), 8.24 (2H, d, J=3Hz)

18) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-cyanophenylmethyl)oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.09-2.20 (2H, m), 2.28 (3H, s), 2.97 (2H, t, J=5Hz), 3.35 (3H, s), 3.65 (3H, s), 4.24 (2H, br), 4.88 (1H, d, J=12Hz), 5.06 (1H, d, J=12Hz), 6.57 (1H, s), 6.67-6.80 (2H, m), 6.95-7.08 (5H, m), 7.35-7.45 (3H, m), 7.62 (2H, d, J=8Hz), 8.11 (1H, d, J=8Hz), 8.30 (1H, d, J=8Hz)

19) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2-dimethylaminoeth-1-yl)oxycarbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.60 (2H, m), 1.67-1.88 (4H, m), 2.05-2.14 (2H, m), 2.27 (9H, s), 2.38 (2H, t, J=6Hz), 2.58 (2H, t, J=5Hz), 2.92 (2H, t, J=5Hz), 3.33 (3H, s), 3.80 (3H, s), 3.86-4.00 (2H, m), 4.19 (2H, t, J=5Hz), 4.30 (2H, t, J=5Hz), 6.57-6.67 (2H, m), 6.87 (1H, dd, J=2, 8Hz), 7.00-7.11 (4H, m), 7.44 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

20) 4-[2-(3-Aminoprop-1-yloxy)benzoyl]amino-3-methoxy-N-(2-hydroxy-4-methylphenyl) -N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.92-2.03 (2H, m), 2.16 (3H, s), 2.75 (2H, t, J=5Hz), 3.20 (3H, s), 3.75 (3H, s), 4.34 (2H, t, J=5Hz), 6.49 (1H, d, J=8Hz), 6.66 (1H, s), 6.87 (1H, d, J=8Hz), 6.92 (1H, d, J=8Hz), 7.12 (1H, dd, J=7, 8Hz), 7.29 (1H, d, J=8Hz), 7.58 (1H, dd, J=2, 8Hz), 8.05 (1H, d, J=8Hz), 8.27 (1H, d, J=8Hz)

21) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(1,5-dimethyl-3-cyanopyrrol-2-yl)phenylmethyl]

oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.00-2.11 (2H, m), 2.14 (3H, s), 2.21 (3H, s), 2.89 (2H, t, J=5Hz), 3.40 (3H, s), 3.45 (3H, s), 3.62 (3H, s), 4.27 (2H, t, J=5Hz), 4.89 (1H, d, J=13Hz), 5.13 (1H, d, J=13Hz), 6.22 (1H, s), 6.68-6.75 (2H, m), 6.89 (1H, d, J=8Hz), 7.00-7.12 (5H, m), 7.38-7.47 (6H, m), 8.19 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

22) 4-[2-(3-Aminoprop-1-yloxy)benzoyl]amino-3-methoxy-N-[2-[4-(N,N-dimethylureido)but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.62-1.88 (4H, m), 1.90-2.15 (2H, m), 2.27 (3H, s), 2.86-2.94 (2H, m), 2.90 (6H, s), 3.22-3.35 (2H, m), 3.31 (3H, s), 3.77 (3H, s), 3.75-3.98 (2H, m), 4.27 (2H, t, J=5Hz), 6.57-6.70 (2H, m), 6.88-7.11 (6H, m), 7.42 (1H, dd, J=2, 8Hz), 8.19 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

23) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[3-(4-methylpiperazin-1-yl)carbonylpyrid-6-yl]methoxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.09-2.20 (2H, m), 2.28 (3H, s), 2.31 (3H, s), 2.34-2.52 (4H, m), 2.96 (2H, t, J=5Hz), 3.40 (3H, s), 3.42-3.50 (2H, m), 3.69 (3H, s), 3.70-3.84 (2H, m), 4.29 (2H, t, J=5Hz), 4.98 (1H, d, J=13Hz), 5.18 (1H, d, J=13Hz), 6.62 (1H, s), 6.72 (1H, d, J=8Hz), 6.98-7.11 (5H, m), 7.26-7.34 (1H, m), 7.45 (1H, dd, J=2, 8Hz), 7.73 (1H, d, J=8Hz), 8.16 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz), 8.63 (1H, s)

24) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(3-dimethylaminoprop-1-yloxycarbonyl)aminobut-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.62-1.87 (6H, m), 2.02-2.11 (2H, m), 2.27 (6H, s), 2.41 (2H, t, J=5Hz), 2.91 (2H, t, J=5Hz), 3.22 (2H, q, J=5Hz), 3.30 (3H, s), 3.78 (3H, s), 3.84-3.95 (2H, m), 4.08 (2H, t, J=5Hz), 4.27 (2H, t, J=5Hz), 6.60-6.66 (2H, m), 6.90 (1H, d, J=8Hz), 6.99-7.10 (3H, m), 7.44 (1H, dd, J=2, 8Hz), 8.18 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

25) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylhomopiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.50-2.18 (8H, m), 2.30 (3H, s), 2.32 (2H, t, J=5Hz), 2.33 (3H, s), 2.53-2.70 (4H, m), 2.93 (2H, t, J=5Hz), 3.35 (3H, s), 3.52-3.72 (4H, m), 3.80 (3H, s), 3.82-4.09 (2H, m), 4.31 (2H, t, J=5Hz), 6.55-6.70 (2H, m), 6.82-7.18 (6H, m), 7.42-7.53 (1H, m), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

26) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2- [5- (2-dimethylaminoethyl)aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-1.60 (2H, m), 1.66-2.15 (8H, m), 2.22 (6H, s), 2.26 (3H, s), 2.41 (2H, t, J=5Hz), 3.22-3.39 (2H, m), 3.31 (3H, s), 3.70-4.00 (2H, m), 3.78 (3H, s), 4.28 (2H, t, J=5Hz), 6.37 (1H, br), 6.59 (2H, br), 6.81-7.13 (6H, m), 7.42 (1H, dd, J=2, 8Hz), 8.18 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

27) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(2-dimethylaminoethyl)-N-methylaminocarbonyl]pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.44-2.21 (8H, m), 2.25 (3H, s), 2.27 (6H, s), 2.29-2.50 (4H, m), 2.91 (1H, s), 3.00 (2H, s), 3.26-3.51 (4H, m), 3.31 (3H, s), 3.77 (3H, br s), 3.81-4.02 (2H, m), 4.22 (2H, t, J=5Hz), 4.88 (1H, br), 6.52-6.68 (2H, br), 6.79-7.11 (5H, m), 7.43-7.50 (1H, m), 8.20 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

28) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(3-dimethylaminoprop-1-yl)carbamoyl]pent-1-yl]oxy-4-methylpehenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.60 (2H, m), 1.63-1.99 (8H, m), 2.03-2.14 (2H, m), 2.21 (2H, t, J=5Hz), 2.24 (6H, s), 2.29 (3H, s), 2.39 (2H, t, J=5Hz), 2.90 (2H, t, J=6Hz), 3.25-3.37 (2H, m), 3.32 (3H, s), 3.79 (3H, s), 3.81-4.01 (2H, m), 4.30 (2H, t, J=5Hz), 6.61 (2H, br), 6.85-7.14 (6H, m), 7.39-7.50 (1H, m), 8.20 (1H, d, J=8Hz), 8.40 (1H, br)

29) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(3-dimethylaminoprop-1-yl)-N-methylcarbamoyl]pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.52-1.94 (6H, m), 2.05-2.14 (2H, m), 2.20 (3H, s), 2.21 (3H, s), 2.26 (3H, s), 2.20-2.45 (6H, s), 2.90 (2H, t, J=5Hz), 2.91 and 2.99 (total 3H, s, rotamer), 3.32 (3H, s), 3.40 (2H, t, J=5Hz), 3.80 (3H, s), 4.31 (2H, t, J=5Hz), 6.55-6.67 (2H, m), 7.41-7.49 (2H, m), 8.21 (1H, d, J=8Hz), 8.42 (1H, d, J=8Hz)

30) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-hydroxypiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.43-1.95 (6H, m), 2.03-2.51 (8H, m), 2.29 (3H, s), 2.94 (2H, t, J=5Hz), 2.98-3.22 (4H, m), 3.32 (3H, s), 3.46-3.58 (1H, m), 3.79 (3H, s), 3.80-4.26 (6H, m), 4.28 (2H, t, J=5Hz), 6.56-6.67 (2H, m), 6.81-7.13 (6H,

m), 7.36 (1H, dd, J=8, 8Hz), 8.10-8.20 (1H, m), 8.33-8.49 (1H, m)

31) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-aminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.51-2.03 (6H, m), 2.09-2.19 (2H, m), 2.27 (3H, s), 2.29-2.42 (4H, m), 2.59-2.71 (2H, m), 2.94 (2H, t, J=5Hz), 2.96-3.11 (3H, m), 3.33 (3H, s), 3.78 (3H, s), 3.85-4.02 (2H, m), 4.22 (2H, t, J=5Hz), 6.55-6.67 (2H, m), 6.81-7.12 (6H, m), 7.44 (1H, dd, J=8, 8Hz), 8.19 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

32) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)-aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.46-1.89 (6H, m), 1.93-2.05 (4H, m), 2.25 (6H, s), 2.49 (2H, t, J=5Hz), 2.52-2.62 (2H, m), 2.79-2.89 (2H, m), 2.92 (2H, t, J=5Hz), 3.31 (3H, s), 3.79 (3H, s), 3.80-4.01 (2H, m), 4.28 (2H, t, J=5Hz), 6.56-6.64 (2H, m), 6.80-7.12 (6H, m), 7.41-7.50 (1H, m), 8.18 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

33) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[bis(2-hydroxyethy-1-yl)-aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.54-1.91 (6H, m), 2.11-2.20 (2H, m), 2.26 (3H, s), 2.38-2.59 (4H, m), 3.40-3.57 (4H, m), 3.61-3.97 (6H, m), 4.22 (2H, t, J=5Hz), 6.60-6.68 (2H, m), 6.88-7.16 (6H, m), 7.44-7.54 (1H, m), 8.12 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

34) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2,2-dimethylhydrazino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.91 (6H, m), 2.06-2.40 (4H, m), 2.28 (3H, s), 2.51 (3H, s), 2.57 (3H, s), 2.92 (2H, t, J=5Hz), 3.32 (3H, s), 3.78 (3H, s), 3.80-4.02 (2H, m), 4.28 (2H, t, J=5Hz), 6.55-6.68 (2H, m), 6.80-7.13 (5H, m), 7.46 (1H, dd, J=8Hz), 8.19 (1H, d, J=8Hz), 8.38 (1H, br)

35) 4- [2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(carbamoylmethylamino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.47-1.58 (2H, m), 1.68-1.85 (4H, m), 2.06-2.17 (2H, m), 2.27 (3H, s), 2.94 (2H, t, J=5Hz), 3.31 (3H, s), 3.80 (3H, s), 3.81-4.00 (2H, m), 3.89 (2H, d, J=5Hz), 4.28 (2H, t, J=5Hz), 5.78 (1H, br), 6.60-6.74 (3H, m), 6.90-7.13 (6H, m), 7.41-7.49 (1H, m), 8.17 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

36) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2-carbamoylethylamino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-1.58 (2H, m), 1.62-1.84 (4H, m), 2.14 (2H, t, J=5Hz), 2.22 (2H, t, J=5Hz), 2.29 (3H, s), 2.40 (2H, t, J=5Hz), 2.98 (2H, br), 3.30 (3H, s), 3.40-3.55 (2H, m), 3.78 (3H, s), 3.80-4.01 (2H, m), 4.27 (2H, t, J=5Hz), 6.58-6.79 (4H, m), 6.88-7.12 (6H, m), 7.41-7.49 (1H, m), 8.16 (1H, d, J=8Hz), 8.39 (1H, d, J=7Hz)

37) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-pyridylaminocarbonyl)pent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.52-1.89 (6H, m), 2.10-2.22 (2H, m), 2.26 (3H, s), 2.45 (2H, br), 2.95 (2H, t, J=5Hz), 3.32 (3H, s), 3.72 (3H, s), 3.82-4.00 (2H, m), 4.27 (2H, t, J=5Hz), 6.57-6.72 (2H, m), 6.90-7.15 (6H, m), 7.46 (1H, dd, J=2, 8Hz), 7.56 (2H, br), 8.12 (1H, d, J=8Hz), 8.35-8.50 (3H, m), 9.46 (1H, br)

38) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[4-(diethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.05 (6H, t, J=5Hz), 1.35-1.95 (10H, m), 2.04-2.13 (2H, m), 2.28 (3H, s), 2.36 (2H, t, J=5Hz), 2.54 (4H, q, J=5Hz), 2.56-2.80 (2H, m), 2.91 (2H, t, J=5Hz), 2.93-3.07 (2H, m), 3.33 (3H, s), 3.80 (3H, s), 3.82-4.03 (2H, m), 4.30 (2H, t, J=5Hz), 6.56-6.68 (2H, m), 6.81-7.12 (6H, m), 7.42-7.49 (1H, m), 8.22 (1H, d, J=7Hz), 8.41 (1H, d, J=8Hz)

39) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[6-(4-methylpiperazin-1-yl)hex-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.45-1.58 (2H, m), 1.62-1.84 (4H, m), 2.14 (2H, t, J=5Hz), 2.29 (3H, s), 2.40 (2H, t, J=5Hz), 2.98 (2H, br), 3.30 (3H, s), 3.40-3.55 (2H, m), 3.78 (3H, s), 3.80-4.01 (2H, m), 4.27 (2H, t, J=5Hz), 6.58-6.79 (4H, m), 7.41-7.49 (1H, m), 8.16 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

40) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(2-pyridyl)phenylmethyl]oxy-4-methylphenyl]-

N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.97-2.08 (2H, m), 2.26 (3H, s), 2.85 (2H, t, J=5Hz), 3.40 (3H, s), 3.62 (3H, s), 4.26 (2H, t, J=5Hz), 4.96 (1H, d, J=12Hz), 5.14 (1H, d, J=12Hz), 6.54-6.62 (2H, m), 6.40 (1H, d, J=7Hz), 6.98-7.14 (5H, m), 7.39 (1H, d, J=8Hz), 7.39-7.49 (1H, m), 7.70 (2H, s), 7.98 (1H, d, J=8Hz), 8.22 (1H, d, J=8Hz), 8.39 (1H d, J=8Hz), 8.68 (1H, br)

41) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-[(4-methylpiperazin-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.62-1.88 (4H, m), 2.30-2.15 (2H, m), 2.28 (6H, s), 2.34-2.42 (4H, m), 2.93 (2H, t, J=5Hz), 3.25-3.48 (6H, m), 3.33 (3H, s), 3.79 (3H, s), 3.79-3.99 (2H, m), 4.30 (2H, t, J=5Hz), 6.58-6.70 (2H, m), 6.90-7.11 (5H, m), 7.45 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

42) 4-[2-(3-Aminoprop-1-yl)oxybenzoylamino]-3-methoxy-N-[2-[4-[(4-dimethylaminopiperidin-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.44-1.98 (8H, m), 2.26 (3H, s), 2.49 (6H, s), 2.66-2.93 (3H, m), 3.05 (2H, t, J=5Hz), 3.25-3.32 (2H, m), 3.29 (3H, s), 3.79 (3H, s), 3.81-3.99 (2H, m), 4.15-4.29 (4H, m), 6.57-6.64 (2H, m), 6.91-7.12 (5H, m), 7.46 (1H, dd, J=2, 8Hz), 8.04 (1H, d, J=8Hz), 8.35 (1H, d, J=8Hz)

Example 47

[0361] The following compound was obtained by using 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide as a starting compound according to a similar manner to that of Example 45.

4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(3-aminoprop-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.87-1.98 (2H, m), 2.00-2.09 (2H, m), 2.25 (3H, s), 2.83-2.96 (4H, m), 3.30 (3H, s), 3.78 (3H, s), 3.87-4.10 (2H, m), 4.27 (2H, t, J=7.5Hz), 6.57-6.66 (2H, m), 6.90 (1H, m), 7.00-7.10 (3H, m), 7.42 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

Example 48

[0362] The following compounds were obtained according to a similar manner to that of Example 47.

1) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-aminoacetylaminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
MASS (m/z) : 592 (M+1)

2) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(piperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.48-1.95 (6H, m), 2.07-2.20 (2H, m), 2.28 (3H, s), 2.32-2.63 (5H, m), 2.75-3.01 (3H, m), 3.21 (3H, s), 3.40-3.64 (4H, m), 3.78 (3H, s), 3.83-4.08 (2H, m), 4.27 (2H, t, J=5Hz), 6.55-6.70 (2H, m), 6.82-7.17 (6H, m), 7.20-7.50 (1H, m), 8.29 (1H, d, J=7Hz), 8.39 (1H, d, J=8Hz)

3) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(3-aminopropionyl)aminobut-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.64-1.88 (4H, m), 2.06-2.19 (2H, m), 2.28 (3H, s), 2.32-2.46 (2H, m), 2.90-3.13 (4H, m), 3.23-3.44 (2H, m), 3.30 (3H, s), 3.77 (3H, s), 3.78-4.01 (2H, m), 4.27 (2H, br), 6.55-6.68 (2H, m), 6.88-7.11 (5H, m), 7.28-7.50 (2H, m), 8.20 (1H, d, J=8Hz) 8.31 (1H, d, J=8Hz)

4) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(piperidin-4-yl)carbonylaminobut-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.60-1.91 (8H, m), 2.09-2.21 (2H, m), 2.28 (3H, s), 2.70 (1H, br), 2.97 (2H, t, J=5Hz), 3.11-3.40 (8H, m), 3.30 (3H, s), 3.72-3.96 (2H, m), 3.78 (3H, s), 4.28 (2H, t, J=5Hz), 6.57-6.65 (2H, m), 6.90-7.08 (4H, m), 7.23-7.28 (2H, m), 7.38-7.49 (2H, m), 8.13 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

5) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-guanidinobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.62-1.80 (4H, m), 2.05-2.14 (2H, m), 2.20 (3H, s), 2.55-2.70 (2H, m), 2.94 (2H, t, J=5Hz), 3.31

(3H, s), 3.62-3.73 (2H, m), 3.72 (3H, s), 4.22 (1H, d, J=5Hz), 6.48 (1H, d, J=8Hz), 6.61 (1H, s), 6.75 (1H, d, J=8Hz), 6.95-7.09 (5H, m), 7.43 (1H, dd, J=2, 8Hz), 8.03 (1H, d, J=8Hz), 8.32 (1H, d, J=8Hz)

Example 49

[0363] A solution of 4-hydroxy-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide (320 mg) in N,N-dimethylformamide (8 ml) was treated with sodium hydride (29.1 mg, 60% w/w in mineral oil) at 0°C. The reaction mixture was stirred at 0°C for 15 minutes and then at ambient temperature for 10 minutes. o-Nitrobenzyl bromide (143 mg) was added, and the reaction mixture was stirred for 2.5 hours. The reaction was quenched with water and the mixture was diluted with ethyl acetate. The organic phase was washed with saturated aqueous sodium hydrogen carbonate, and brine. The organic solution was dried over magnesium sulfate, concentrated, and purified by silica gel column chromatography (SiO_2 15 g, 3% methanol in dichloromethane) to give 3-methoxy-4-(2-nitrobenzyloxy)-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (210 mg).

NMR ($CDCl_3$, δ) : 1.43-1.59 (2H, m), 1.61-1.88 (4H, m), 2.21-2.44 (12H, m), 3.31 (3H, s), 3.42-3.52 (2H, m), 3.56-3.67 (2H, m), 3.71 (3H, s), 3.78-4.00 (2H, m), 5.46 (3H, s), 6.52-6.67 (3H, m), 6.77-6.91 (2H, m), 6.95 (1H, br s), 7.46 (1H, m), 7.64 (1H, m), 7.84 (1H, d, J=8Hz), 8.14 (1H, d, J=8Hz)

Example 50

[0364] To a solution of 4-[2-(3-aminopropylthio)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yloxy]phenyl]benzamide (160 mg) in methanol (5 ml) was added a suspension of sodium metaperiodate (50.6 mg) and 5 ml of water. The mixture was stirred for 20 hours at ice-bath temperature and diluted with chloroform. The lower chloroform layer was removed, and the water layer was extracted with chloroform. The combined organic extracts were dried over anhydrous sodium sulfate. The solvent was removed at reduced pressure, and purified by preparative thin layer chromatography (methanol/dichloromethan/ammonia = 10/90/2) co give free amine (70 mg). To a solution of this amine in ethanol (3 ml) was added 1N hydrochloric acid (0.2 ml) and stirred for 5 minutes. The solution was concentrated to give 4-[2-(3-aminopropylsulfinyl)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride.

NMR (DMSO-d_6, δ) : 1.38-1.67 (4H, m), 1.68-1.88 (2H, m), 1.94-2.13 (2H, m), 2.22 (3H, s), 2.40 (2H, t, J=7Hz), 2.69-3.12 (9H, m), 3.12-3.58 (7H, m), 3.62 (3H, s), 3.80-4.17 (3H, m), 4.43 (1H, m), 6.64 (1H, d, J=8Hz), 6.83 (1H, s), 6.91 (2H, br s), 7.04 (1H, d, J=8Hz), 7.53 (1H, m), 7.68 (1H, dd, J=8, 8Hz), 7.85 (1H, dd, J=8, 8Hz), 7.90-8.19 (3H, s), 9.84 (1H, s)

Example 51

[0365] To a solution of 3-methoxy-4-[2-[3-(phthalimido)prop-1-yl]thiobenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (150 mg) in dichloromethane (10 ml) was added m-chloroperbenzoic acid (80.3 mg) and the mixture was stirred at ambient temperature for 2 hours. The solution was washed successively with saturated aqueous sodium hydrogen carbonate, water and brine, and the organic phase was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by silica gel column (2% methanol in chloroform) to give 3-methoxy-4-[2-[3-(phthalimido)prop-1-yl]sulfonylbenzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (150 mg).

MASS (m/z) : 839 (M+1)

Example 52

[0366] A solution of 4-[2-[2-[(3-aminioprop-1-yl)oxy]phenyl]-vinyl]-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (100 mg), 20% palladium hydroxide (30 mg) in methanol (5 ml) was stirred under atmospheric pressure of hydrogen at ambient temperature. After 12 hours, the reaction mixture was filtered through a bed of Celite, and the solvent was removed by rotary evaporation and the crude product was purified by NH-silica gel (chromatorex) column chromatography (SiO_2 10 g, 1% methanol in chloroform) to give free amine. To the solution of amine (80 mg) in ethanol (3 ml) was added 1N hydrochloric acid (0.25 ml) and stirred for 5 minutes. The solution was evaporated to give 4-[2-[2-[(3-aminoprop-1-yl)oxy]phenyl]ethyl]-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride (70 mg).

NMR (DMSO-d_6, δ) : 1.36-1.65 (4H, m), 1.65-1.82 (2H, m), 1.97-2.13 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7Hz), 2.58-3.11 (13H, m), 3.17 (3H, s), 3.26-3.68 (5H, m), 3.72-4.21 (5H, m), 4.42 (1H, m), 6.63 (1H, d, J=8Hz), 6.70-7.05 (8H, m), 7.13 (1H, dd, J=8, 8Hz), 8.00-8.24 (2H, m)

Example 53

[0367] The following compounds were obtained according to a similar manner to that of Example 10.

1) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-(4-hydroxyphenyl) benzamide
NMR ($CDCl_3$, δ) : 1.43 (9H, s), 1.60-1.68 (2H, m), 3.16-3.25 (2H, m), 3.49 (3H, s), 3.63 (3H, s), 4.16-4.23 (2H, m), 4.73-4.80 (1H, br), 6.67-6.74 (3H, m), 6.84-7.01 (5H, m), 7.07-7.14 (2H, m), 7.47 (1H, t, J=8Hz), 8.16 (1H, d, J=8Hz), 8.52 (1H, d, J=8Hz)
ESI-MASS (m/z) : 550 (M+H)

2) 3-Methoxy-4-[2-[1-(tert-butoxycarbonyl)piperidin-4-yl]oxybenzoyl]amino-N-(2-hydroxy-4-methyl)phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.43 (9H, s), 1.68-2.10 (4H, m), 2.23 (3H, s), 2.96-3.17 (2H, m), 3.36 (3H, s), 3.64-3.98 (5H, m), 4.60 (1H, m), 6.36-7.03 (7H, m), 7.10 (1H, t, J=7Hz), 7.43 (1H, t, J=7Hz), 8.19 (1H, d, J=7Hz)

3) 4-[2-(3-Amino-1-methylprop-1-yl)oxybenzoyl]amino-3-methoxy-N-(2-hydroxy-4-methyl)phenyl-N-methylbenzamide
NMR (DMSO-d_6, δ) : 1.33 (3H, d, J=7.5Hz), 1.63-1.76 (1H, m), 1.87-1.98 (1H, m), 2.14 (3H, s), 2.65 (2H, t, J=7.5Hz), 3.18 (3H, s), 3.74 (3H, s), 4.96 (1H, m), 6.47 (1H, d, J=7Hz), 6.63 (1H, s), 6.86 (1H, d, J=7Hz), 7.91 (1H, d, J=7Hz), 7.01 (1H, s), 7.09 (1H, t, J=7Hz), 7.32 (1H, d, J=7Hz), 7.52 (1H, t, J=7Hz), 8.04 (1H, d, J=7Hz), 8.30 (1H, d, J=7Hz)

4) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)amino-1-methylprop-1-yl]oxybenzoyl]amino-N-(2-hydroxy-4-methyl) phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.36 (3H, d, J=7.5Hz), 1.40 (9H, s), 1.80-2.10 (2H, m), 2.22(3H, s), 3.16-3.28 (2H, m), 3.35 (3H, s), 3.69 (3H, s), 4.64 (1H, m), 4.79 (1H, br), 6.52 (1H, m), 6.70-6.82 (2H, m), 6.91-7.11 (4H, m), 7.41 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.47 (1H, m)

5) 4-(2-Hydroxybenzoylamino-3-methoxy-N-(2-hydroxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 2.26 (3H, s), 3.36 (3H, s), 6.56 (1H, m), 6.65-6.86 (4H, m), 6.96-7.08 (2H, m), 7.35-7.44 (2H, m), 8.20 (1H, br), 8.61 (1H, br)

6) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-(2-hydroxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.42 (9H, s), 1.68 (2H, br), 1.99 (2H, br), 2.22 (3H, s), 3.19 (2H, br), 3.39 (3H, s), 3.49 (2H, br), 5.03 (1H, br), 6.43-6.72 (6H, m), 7.08 (2H, br), 7.39 (1H, br), 8.21 (1H, d, J=8Hz), 8.45 (1H, br)

Example 54

[0368] The following compounds were obtained according to a similar manner to that of Example 12.

1) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-(5-ethoxycarbonylpent-1-yloxy)phenyl]benzamide
NMR ($CDCl_3$, δ) : 1.21-1.29 (3H, m), 1.40 (9H, s), 1.42-1.90 (8H, m), 2.09-2.19 (2H, m), 3.27-3.34 (2H, m), 3.47 (3H, s), 3.82 (3H, s), 3.89 (2H, t, J=8Hz), 4.08-4.17 (2H, m), 4.26 (2H, t, J=8Hz), 4.70-4.77 (1H, br), 6.75 (2H, d, J=8Hz), 6.83 (1H, d, J=8Hz), 6.94-7.02 (3H, m), 7.07-7.13 (2H, m), 7.46 (1H, t, J=8Hz), 8.21 (1H, d, J=8Hz), 8.42 (1H, d, J=8Hz)
ESI-MASS (m/z) : 692 (M+H)

2) 4-[2-Benzyloxy)benzoyl]amino-N-[2-(3-ethoxycarbonylprop-1-yl)oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 2.03-2.17 (2H, m), 2.50 (2H, t, J=7.5Hz), 3.32 (3H, s), 3.87-4.04 (2H, m), 4.16 (2H, q, J=7.5Hz), 5.19 (2H, s), 6.78 (2H, d, J=8Hz), 6.92-7.00 (3H, m), 7.07-7.21 (5H, m), 7.38-7.53 (6H, m), 8.26 (1H, d, J=7Hz)

3) 4-(2-Iodobenzoyl)amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.24 (3H, t, J=7.5Hz), 1.42-1.55 (2H, m), 1.63-1.72 (2H, m), 1.76-1.88 (2H, m), 2.31 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.81-3.99 (2H, m), 4.11 (2H, q, J=7.5Hz), 6.76-6.83 (2H, m), 7.00 (1H, d, J=7Hz), 8.08-7.17 (2H, m), 7.29-7.49 (5H, m), 7.66 (1H, s), 7.88 (1H, d, J=7Hz)

4) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]-oxybenzoyl]amino-N-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.41 (9H, s), 1.93-1.97 (2H, m), 2.07-2.17 (2H, m), 2.26 (3H, s), 3.22-3.32 (4H, m), 3.30 (3H, s), 3.78 (3H, s), 3.82-4.05 (2H, m), 6.60-6.66 (2H, m), 6.86-6.91 (2H, m), 7.00 (1H, d, J=7Hz), 7.03-7.10 (2H, m), 7.43 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

5) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-methyl-N-[4-methyl-2-[4-(phthalimido)but-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.85-1.92 (2H, m), 2.10-2.17 (2H, m), 2.27 (3H, s), 3.22-3.32 (2H, m), 3.28 (3H, s), 3.74-3.81 (2H, m), 3.81 (3H, s), 3.92-4.15 (2H, m), 4.24 (2H, t, J=7.5Hz), 6.57-6.65 (2H, m), 6.83-6.90 (2H, m), 6.97-7.14 (3H, m), 7.24 (1H, t, J=7Hz), 7.69-7.77 (2H, m), 7.82-7.91 (2H, m), 8.21 (1H, d, J=7Hz), 8.40 (1H, d, J=7Hz)

6) 3-Methoxy-4-[2-[1-(tert-butoxycarboyl)piperidin-4-yl]oxybenzoyl]amino-N-[2-(5-ethoxycarbonylpent-1-yl) oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7.5Hz), 1.42-1.91 (6H, m), 1.45 (9H, s), 2.02 -2.12 (2H, m), 2.27 (3H, s), 2.27-2.88 (2H, m), 2.97-3.18 (2H, m), 3.32 (3H, s), 3.40 (2H, t, J=7Hz), 3.74 (3H, s), 3.89-4.00 (2H, m), 4.13 (2H, q, J=7.5Hz), 4.66 (1H, m), 6.59 (1H, d, J=7Hz), 6.61 (1H, s, J=7Hz), 6.80-6.92 (2H, m), 6.98-7.12 (3H, m), 7.43 (1H, t, J=7Hz), 8.19 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

7) 3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)amino-1-methyl-prop-1-yl]oxybenzoyl]amino-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.24 (3H, t, J=7.5Hz), 1.38 (9H, s), 1.40 (2H, d, J=7.5Hz), 1.41-2.10 (8H, m), 2.26 (3H, s), 2.27-2.33 (2H, m), 3.23-3.30 (2H, m), 3.30 (3H, s), 3.79 (3H, s), 3.83-3.99 (2H, m), 4.12 (2H, q, J=7.5Hz), 4.62-4.77 (2H, m), 6.58-6.63 (2H, m), 6.82 (1H, t, J=7Hz), 7.01 (1H, d, J=7Hz), 7.05-7.12 (2H, m), 7.43 (1H, t, J=7Hz), 8.21 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

8) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-(2-methoxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.08-2.20 (2H, m), 2.29 (3H, s), 3.28 (2H, q, J=5Hz), 3.31 (3H, s), 3.75 (3H, s), 3.80 (3H, s), 4.25 (2H, t, J=5Hz), 4.74 (1H, br), 6.59-6.65 (2H, m), 6.89 (1H, d, J=8Hz), 7.00 (1H, d, J=8Hz), 7.06-7.13 (2H, m), 7.46 (1H, dd, J=2, 8Hz), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

9) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[4-(2-pyridyl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.39 (9H, s), 2.09 (2H, t, J=5Hz), 2.29 (3H, s), 3.27 (2H, q, J=5Hz), 3.40 (3H, s), 3.61 (3H, s), 4.21 (2H, t, J=5Hz), 4.82 (1H, br), 4.97 (1H, d, J=12Hz), 5.14 (1H, d, J=12Hz), 6.55-6.74 (2H, m), 6.89-7.12 (7H, m), 7.19-7.24 (1H, m), 7.39 (1H, d, J=8Hz), 7.41-7.49 (1H, m), 7.70 (2H, s), 7.99 (1H, d, J=8Hz), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz), 8.67 (1H, d, J=5Hz)

10) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[4-(1,5-dimethyl-3-cyano-pyrrol-2-yl)phenylmethyl]oxy-4-methylphenyl)-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.03-2.15 (2H, m), 2.13 (3H, s), 2.30 (3H, s), 3.26 (2H, q, J=5Hz), 3.40 (3H, s), 3.46 (3H, s), 3.58 (3H, s), 4.19 (2H, t, J=5Hz), 4.86 (1H, d, J=12Hz), 5.10 (1H, d, J=12Hz), 6.65-6.73 (2H, m), 6.82 (1H, d, J=8Hz), 6.95-7.10 (4H, m), 7.34-7.44 (6H, m), 8.00 (1H, s), 8.19 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

11) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-[4-(thiazol-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.05-2.16 (2H, m), 3.27 (2H, q, J=5Hz), 3.40 (3H, s), 3.62 (3H, s), 4.20 (2H, t, J=5Hz), 4.76 (1H, br), 4.89 (1H, d, J=12Hz), 5.07 (1H, d, J=12Hz), 6.62-6.72 (2H, m), 6.89 (1H, d, J=8Hz), 6.96-7.11 (4H, m), 7.28 (1H, d, J=3Hz), 7.31 (2H, d, J=8Hz), 7.42 (1H, dd, J=2, 8Hz), 7.81 (1H, d, J=8Hz), 7.93 (2H, d, J=8Hz), 8.00 (1H, s), 8.20 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

12) 4-[2-[3-(tert-Butoxycarbonylamio)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-[4-(oxazol-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.05-2.16 (2H, m), 2.29 (3H, s), 3.27 (2H, q, J=5Hz), 3.40 (3H, s), 3.65 (3H, s), 4.21 (2H, t, J=5Hz), 4.78 (1H, br), 4.90 (1H, d, J=13Hz), 5.10 (1H, d, J=13Hz), 6.64 (1H, s), 6.70 (1H, d, J=8Hz), 6.85 (1H, d, J=8Hz), 6.98-7.17 (5H, m), 7.20 (1H, s), 7.30-7.49 (3H, m), 7.63 (1H, s), 8.03 (1H, d, J=8Hz), 8.22 (1H, d,

J=8Hz), 8.40 (1H, d, J=8Hz)

13) 4-[2-[3- (tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-[4-(pyrimidin-2-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 2.05-2.16 (2H, m), 2.28 (3H, s), 3.28 (2H, q, J=5Hz), 3.40 (3H, s), 3.65 (3H, s), 4.22 (2H, t, J=5Hz), 4.78 (1H, br), 4.95 (1H, d, J=12Hz), 5.14 (1H, d, J=12Hz), 6.65-6.70 (2H, m), 6.88 (1H, d, J=8Hz), 6.96-7.19 (5H, m), 7.38-7.46 (3H, m), 8.21 (1H, d, J=8Hz), 8.35-8.44 (3H, m), 8.74 (1H, d, J=3Hz)

14) 4-[2-[3- (tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-(4-cyanophenylmethyl)oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.41 (9H, s), 2.08-2.20 (2H, m), 2.30 (3H, s), 3.30 (2H, q, J=5Hz), 3.40 (3H, s), 3.68 (3H, s), 4.26 (2H, t, J=5Hz), 4.89 (1H, d, J=13Hz), 5.09 (1H, d, J=13Hz), 6.60 (1H, s), 6.73 (1H, d, J=8Hz), 6.98-7.12 (5H, m), 7.39-7.52 (3H, m), 7.68 (1H, d, J=8Hz), 8.20 (1H, d, J=8Hz), 8.34 (1H, d, J=8Hz)

15) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-(4-phthalimidobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.72-1.95 (4H, m), 2.08-2.19 (2H, m), 2.29 (3H, s), 3.31 (2H, q, J=5Hz), 3.33 (3H, s), 3.79 (2H, t, J=5Hz), 3.81 (3H, s), 3.84-4.06 (2H, m), 4.25 (2H, t, J=5Hz), 4.82 (1H, br), 6.57 (1H, d, J=8Hz), 6.62 (1H, s), 6.81-6.89 (2H, m), 6.97 (1H, d, J=8Hz), 7.04-7.10 (2H, m), 7.40-7.48 (1H, m), 7.68-7.74 (2H, m), 7.81-7.89 (2H, m), 8.20 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

16) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-(3-methoxycarbonylpyrid-6-yl)methoxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.39 (9H, s), 2.07-2.16 (2H, m), 2.27 (3H, s), 3.29 (2H, q, J=5Hz), 3.42 (3H, s), 3.63 (3H, s), 3.89 (3H, s), 4.24 (2H, t, J=5Hz), 4.95 (1H, d, J=12Hz), 5.08 (1H, d, J=12Hz), 6.58 (1H, s), 6.73 (1H, d, J=8Hz), 6.89 (1H, d, J=8Hz), 6.98 (2H, d, J=8Hz), 7.05-7.12 (3H, m), 7.34 (1H, d, J=8Hz), 7.44 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.28 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz), 9.14 (1H, s)

Example 55

[0369] The following compound was obtained according to a similar manner to that of Example 35.
4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl-amino-3-methoxy-N-[2-[4-(tert-butoxycarbonylguanidino)but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.43 (9H, s), 1.44 (9H, s), 1.52-1.60 (2H, m), 1.65-1.74 (2H, m), 1.92-2.07 (2H, m), 2.21 (3H, s), 3.10-3.25 (4H, m), 3.38 (3H, s), 3.50 (2H, br), 3.66 (3H, br), 3.78-4.05 (2H, m), 6.49 (2H, br), 6.63-6.82 (3H, m), 7.01-7.10 (2H, m), 7.38 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.44 (1H, br)

Example 56

[0370] The following compounds were obtained according to a similar manner to that of Example 10.

1) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-hydroxy-N-methyl-N-cyclohexylbenzamide
NMR ($CDCl_3$, δ) : 1.07-1.17 (2H, m), 1.41 (9H, s), 1.47-1.76 (8H, m), 2.10-2.20 (2H, m), 2.92-3.00 (2H, m), 3.36-3.44 (2H, m), 3.49 (3H, s), 4.19-4.27 (2H, m), 4.98-5.06 (1H, br), 6.87-6.92 (1H, br), 6.98-7.03 (2H, m), 7.12 (1H, t, J=8Hz), 7.47 (1H, t, J=8Hz), 8.12-8.22 (1H, br), 8.28 (1H, d, J=8Hz), 9.72-9.80 (1H, br)
ESI-MASS (m/z) : 526 (M+H)

2) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-hydroxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.42 (9H, s), 1.50-1.90 (8H, m), 2.20-2.22 (2H, m), 2.27 (3H, s), 2.32 (3H, s), 2.35-2.53 (6H, m), 3.29 (3H, s), 3.32-3.42 (2H, m), 3.50-3.66 (3H, m), 3.72 (2H, br), 3.89 (1H, br), 4.20 (2H, t, J=6Hz), 5.29 (1H, br), 6.54 (1H, s), 6.67 (1H, d, J=7Hz), 6.72 (1H, br), 6.96-7.10 (4H, m), 7.40-7.47 (1H, m), 8.10 (1H, br), 8.27 (1H, d, J=6Hz)

Example 57

[0371] To a solution of 4-[(2-benzyloxy)benzoyl]amino-3-[(2-benzyloxy)benzoyl]oxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (1.2 g) in ethanol (20 ml) was added 1N sodium hy-

droxide solution (10 ml) and the mixture was stirred at ambient temperature for 2 hours. The mixture was concentrated in vacuo and the solution was adjusted to pH 7 with 1N hydrochloric acid. The solution was extracted with ethyl acetate (20 ml) and the organic layer was washed with brine (20 ml). The organic layer was dried over magnesium sulfate and the solution was concentrated in vacuo to give 4-[(2-benzyloxy)benzoyl]amino-3-hydroxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (930 mg)

NMR ($CDCl_3$, δ) : 1.48-1.59 (2H, m), 1.70 (4H, br), 2.29-2.42 (13H, m), 3.29 (3H, s), 3.48 (2H, br), 3.53 (2H, br), 3.80 (1H, br), 3.90 (1H, br), 5.28 (2H, s), 6.53-6.65 (3H, m), 6.72 (1H, br), 6.90-7.12 (4H, m), 7.34-7.37 (3H, m), 7.40-7.49 (4H, m), 8.20-8.27 (1H, m)

Example 58

[0372] The following compounds were obtained according to a similar manner to that of Example 12.

1) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-ethoxycarbonylmethoxy-N-methyl-N-cyclohexylbenzamide
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=8Hz), 1.41 (9H, s), 1.45-1.85 (10H, m), 2.07-2.12 (2H, m), 2.86-3.06 (3H, br), 3.25-3.32 (2H, m), 4.22-4.33 (4H, m), 4.76 (2H, s), 4.98-5.07 (1H, br), 6.91 (1H, s), 7.01-7.15 (3H, m), 7.48 (1H, t, J=8Hz), 8.23 (1H, d, J=8Hz), 8.69 (1H, d, J=8Hz)
ESI-MASS (m/z) : 634 (M+Na)

2) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-isopropoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.19-1.28 (6H, m), 1.38 (9H, s), 1.46-1.58 (2H, m), 1.65-1.88 (6H, m), 1.99-2.10 (2H, m), 2.25 (3H, s), 2.29 (3H, s), 2.32-2.42 (6H, m), 3.15-3.23 (2H, m), 3.31 (3H, s), 3.45-3.50 (2H, m), 3.60-3.64 (2H, m), 3.84-3.97 (2H, m), 4.24-4.36 (3H, m), 6.56-6.65 (2H, m), 6.85 (1H, d, J=7Hz), 6.94-7.02 (3H, m), 7.10 (1H, t, J=6Hz), 7.47 (1H, t, J=7Hz), 8.15 (1H, d, J=7Hz), 8.41 (1H, d, J=7Hz)

3) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-3-propoxybenzamide
NMR ($CDCl_3$, δ) : 0.97 (3H, t, J=7Hz), 1.42 (9H, s), 1.47-1.58 (2H, m), 1.67-1.88 (8H, m), 1.98-2.10 (2H, m), 2.27 (3H, s), 2.28 (3H, s), 2.31-2.41 (6H, m), 3.16-3.26 (2H, m), 3.31 (3H, s), 3.45-3.50 (2H, m), 3.58-3.65 (2H, m), 3.84-3.97 (4H, m), 4.26 (2H, t, J=7Hz), 6.58 (1H, d, J=7Hz), 6.64 (1H, s), 6.84 (1H, d, J=6Hz), 6.95 (1H, d, J=7Hz), 6.99-7.03 (2H, m), 7.09 (1H, t, J=7Hz), 7.45 (1H, t, J=7Hz), 8.16 (1H, d, J=7Hz), 8.38 (1H, d, J=7Hz)

4) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-(3-ethoxycarbonylprop-1-yl)oxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.11 and 1.23 (total 3H, t, J=6Hz), 1.40 (9H, s), 1.48-1.60 (2H, m), 1.60-1.75 (4H, m), 1.75-1.88 (2H, m), 1.98-2.10 (4H, m), 2.26 (3H, s), 2.29 (3H, s), 2.32-2.42 (8H, m), 3.18-3.28 (2H, m), 3.30 (3H, s), 3.45-3.50 (2H, m), 3.62 (2H, br), 3.88-4.10 (5H, m), 4.27 (2H, t, J=6Hz), 6.57 (1H, d, J=7Hz), 6.63 (1H, s), 6.82 (1H, d, J=7Hz), 6.87-6.92 (1H, m), 6.98-7.10 (3H, m), 7.42 (1H, t, J=6Hz), 8.10-8.13 (1H, m), 8.37 (1H, d, J=7Hz)

5) 4-[2-[((3-tert-Butoxycarbonylaminoprop-1-yl)oxy]-benzoyl]amino-3-ethoxycarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=7Hz), 1.39 (9H, s), 1.46-1.90 (8H, m), 2.00-2.10 (2H, m), 2.28 (3H, s), 2.29 (3H, s), 2.30-2.42 (6H, m), 3.18-3.29 (2H, m), 3.30 (3H, s), 3.42-3.50 (2H, m), 3.58-3.65 (2H, m), 3.85-3.97 (2H, m), 4.18-4.29 (4H, m) , 4.52 (2H, s), 6.52-6.13 (2H, m), 6.80 (1H, d, J=7Hz), 6.89-6.99 (3H, m), 7.38-7.48 (1H, m), 8.15 (1H, d, J=7Hz), 8.41 (1H, d, J=7Hz)

6) 4-[(2-Benzyloxy)benzoyl]amino-3-ethoxyl-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
NMR ($CDCl_3$, δ) : 1.08 (3H, t, J=6Hz), 1.45-1.57 (2H, m), 1.60-1.75 (2H, m), 1.77-1.87 (2H, m), 2.25 (3H, s), 2.29 (3H, s), 2.31-2.39 (7H, m), 3.30 (3H, s), 3.46-3.49 (2H, m), 3.60-3.63 (2H, m), 3.70-3.80 (2H, m), 3.82-3.98 (2H, m), 5.34 (2H, s), 6.52-6.60 (2H, m), 6.80-7.10 (5H, m), 7.27-7.38 (6H, m), 8.20-8.22 (1H, m), 8.38-8.43 (1H, m)

Example 59

[0373] The following compounds were obtained according to a similar manner to that of Example 4.

1) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-carboxymethoxy-N-methyl-N-cyclohexyl-benzamide
NMR (CDC13, δ) : 1.03-1.17 (2H, m), 1.39 (9H, s), 1.45-1.85 (8H, m), 2.03-2.12 (2H, m), 2.85-2.98 (3H, m), 3.21-3.33 (2H, m), 4.23-4.31 (2H, m), 4.73 (3H, s), 5.08-5.13 (1H, br), 6.98-7.07 (3H, m), 7.10 (1H, t, J=8Hz), 7.48 (1H, t, J=8Hz), 8.18-8.24 (1H, m), 8.56-8.61 (1H, m)
ESI-MASS (m/z) : 606 (M+Na)

2) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-carboxymethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.38-1.49 (2H, m), 1.49-1.62 (2H, m), 1.67-1.78 (2H, m), 2.02-2.34 (13H, m), 2.78-2.89 (2H, m), 3.38-3.43 (4H, m), 3.58 (3H, s), 3.89-3.96 (2H, m), 4.00-4.18 (2H, m), 4.30 (2H, br), 6.62 (1H, d, J=6Hz), 6.72-6.87 (3H, m), 6.89-6.97 (1H, m), 7.11 (1H, t, J=7Hz), 7.19 (1H, d, J=7Hz) 7.54 (1H, t, J=6Hz), 7.94 (1H, d, J=6Hz), 8.22 (1H, d, J=7Hz)

3) 4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-carboxymethoxy-N-methyl-N- [2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide
MASS (m/z) : 804 (M+H)

Example 60

[0374] To a mixture of 4-(2-iodobenzoyl)amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (1.12 g) and 3-butyn-1-ol (153 mg) in a mixture of tetrahydrofuran (15 ml) and ethylamine (15 ml) were added bis(triphenylphosphine)palladium(II) chloride (23.5 mg) and copper (I) iodide (3.19 mg) and the mixture was refluxed for 8 hours. The solution was diluted with chloroform (50 ml) and the solution was washed with water and brine. The solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an oil. The oil was purified by silica gel column (2% methanol in chloroform) to give 4-[2-(4-hydroxy-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (755 mg) .

NMR ($CDCl_3$, δ) : 1.44-1.57 (2H, m), 1.61-1.86 (4H, m), 2.27 (3H, s), 2.29-2.40 (6H, m), 2.70 (2H, t, J=7.5Hz), 3.33 (3H, s), 3.44-3.49 (2H, m), 3.53-3.60 (2H, m), 3.74 (2H, t, J=7.5Hz), 3.79-3.99 (2H, m), 6.76-6.84 (2H, m), 7.06 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz), 7.34 (2H, d, J=8Hz), 7.40-7.47 (2H, m), 7.48-7.56 (3H, m), 7.99 (1H, m), 9.19 (1H, s)

Example 61

[0375] To an ice cooled solution of 4-[2-(4-hydroxy-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (755 mg) in dichloromethane (20 ml) were added triethylamine (150 mg) and methanesulfonyl chloride (156 mg), and the mixture was stirred in an ice bath for 2 hours. The solution was washed successively with water, 10% hydrochloric acid, saturated aqueous sodium hydrogen carbonate and brine, and the organic phase was dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-[2-(4-methanesulfonyloxy-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (789 mg) .

NMR ($CDCl_3$, δ) : 1.49-1.60 (2H, m), 1.67-1.86 (2H, m), 1.87-1.90 (2H, m), 2.37 (2H, t, J=7.5Hz), 2.68 (3H, s), 2.86-3.06 (6H, m), 2.92 (3H, s), 3.31 (3H, s), 3.77-4.02 (6H, m), 4.32 (2H, t, J=7.5Hz), 6.77-6.87 (2H, m), 7.04 (1H, d, J=7Hz), 7.17 (1H, t, J=7Hz), 7.32 (2H, d, J=8Hz), 7.41-7.53 (5H, m), 7.90 (1H, m), 8.86 (1H, s)

Example 62

[0376] The following compounds were obtained according to a similar manner to that of Example 61.

1) 4-[2-(4-Methanesulfonyloxybut-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
MASS (m/z) : 693 (M+1)

2) 4-[2-(3-Methanesulfonyloxyprop-1-yl)thiobenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.48-1.60 (2H, m), 1.65-1.74 (2H, m), 1.75-1.86 (2H, m), 1.98-2.07 (2H, m), 2.26 (3H, s), 2.30-2.39 (2H, m), 2.70-2.78 (4H, m), 2.79-3.42 (2H, m), 2.90 (3H, s), 2.95-3.07 (2H, m),3.26 (3H, s), 3.71 (3H, s), 3.80-4.01 (4H, m), 4.29 (2H, t, J=7.5Hz), 6.56-6.66 (2H, m), 6.82-7.00 (3H, m), 7.30 (1H, m), 7.39-7.47 (2H, m), 7.60 (1H, d, J=7Hz), 8.27 (1H, d, J=7Hz), 8.58 (1H, s)

Example 63

[0377] A mixture of 4-[2-(4-methanesulfonyloxy-1-butyn-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (800 mg) and potassium phthalimide (430 mg) in dimethyl sulfoxide (20 ml) was stirred at 60°C for 5 hours, and the solution was diluted with ethyl acetate (60 ml). The solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-[2-[4-(phthalimido)-1-butyn-1-yl]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (620 mg).

NMR ($CDCl_3$, δ) : 1.50-1.61 (2H, m), 1.67-1.92 (6H, m), 2.30 (3H, s), 2.33-2.44 (6H, m), 3.38 (3H, s), 3.48-3.52 (2H, m), 3.60-3.67 (2H, m), 3.84-4.01 (4H, m), 6.78-6.85 (2H, m), 7.02 (1H, d, J=7Hz), 7.09-7.19 (2H, m), 7.30-7.70 (6H, m), 7.70-7.77 (2H, m), 7.81-7.90 (2H, m), 8.18 (1H, m)

Example 64

[0378] The following compounds were obtained according to a similar manner to that of Example 63.

1) 4-[2-[4-(Phthalimido)but-1-yl]benzoyl]amino-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenyl-N-methylbenzamide
MASS (m/z) : 693 (M+1)

2) 3-Methoxy-4-[2-[3-(phthalimido)prop-1-yl]thiobenzoyl]-amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
NMR ($CDCl_3$, δ) : 1.47-1.59 (2H, m), 1.61-1.74 (2H, m), 1.78-1.87 (2H, m), 1.92-2.03 (2H, m), 2.26 (3H, s), 2.29 (3H, s), 2.31-2.42 (6H, m), 2.94 (2H, t, J=7.5Hz), 3.31 (3H, s), 3.45-3.53 (2H, m), 3.58-3.67 (2H, m), 3.69-3.81 (2H, m), 3.73 (3H, s), 3.84-4.00 (2H, m), 6.55-6.66 (2H, m), 6.80-6.92 (2H, m), 7.02 (1H, s), 7.27 (1H, m), 7.34-7.44 (2H, m), 7.60-7.90 (5H, m), 8.25 (1H, d, J=7Hz), 8.82 (1H, s)

Example 65

[0379] To an ice cooled mixture of 4-[2-(4-amino-1-butyn-1-yl)benzoyl] amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide (310 mg), nickel chloride hexahydrate (181 mg) in a mixture of tetrahydrofuran (5 ml) and methanol (5 ml) was added sodium borohydride (96.2 mg) in small portions and the mixture was stirred at the same temperature for 2 hours. The mixture was filtered through bed of Celite and the filtrate was evaporated in vacuo. The residue was dissolved in chloroform (20 ml)and washed with water and brine. The organic solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give a syrup. The residue was purified by silica gel column (chloroform:methanol:ammonia = 100:10:1) to give 4-[2-(4-aminobut-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-l-yl)carbonylpent-1-yl]oxy]phenylbenzamide (295 mg).
MASS (m/z) : 597 (M+1)

Example 66

[0380] The following compound was obtained according to a similar manner to that of Example 65.
4-[2-(4-hydroxybut-1-yl)benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide
MASS (m/z) : 615 (M+1)

Example 67

[0381] A mixture of 4-amino-3-methoxy-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]-phenylbenzamide (200 mg) and salicyl aldehyde (48.6 mg) in methanol (10 ml) was refluxed overnight in the presence of 3Å molecular sieves (100 mg). The solution was filtered and the filtrate was treated with sodium borohydride (15.1 mg) at 5°C for 2 hours. The reaction mixture was diluted with chloroform (20 ml) and the solution was washed with water and brine. The organic solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give a crude oil. The product was purified by silica gel column (2% methanol in chloroform) to give 3-methoxy-4-(2-hydroxyphenyl)methylamino-N-methyl-N-[4-methyl-2-[4-(4-methylpiperazin-1-yl)carbonyl]phenylmethoxy]phenylbenzamide (152 mg).

NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.32 (3H, s), 2.32-2.59 (4H, m), 3.34 (3H, s), 3.40-3.55 (2H, m), 3.52 (3H, s), 3.75-3.88 (2H, m), 4.25-4.34 (2H, m), 4.63 (1H, br), 4.42 (1H, d, J=14Hz), 5.08 (1H, d, J=14Hz), 6.43 (1H, d, J=7Hz),

6.62 (1H, s), 6.70 (1H, d, J=7Hz), 6.80-6.88 (4H, m), 7.00 (1H, d, J=7Hz), 7.09-7.18 (2H, m), 7.28 (2H, d, J=8Hz), 7.38 (2H, d, J=8Hz)

Example 68

[0382] The following compound was obtained according to a similar manner to that of Example 67.

3-Methoxy-4- (2-hydroxyphenyl)methylamino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy]phenylbenzamide

NMR ($CDCl_3$, δ) : 1.41-1.52 (2H, m), 1.60-1.69 (2H, m), 1.70-1.80 (2H, m), 2.25 (3H, s), 2.29 (3H, s), 2.30-2.43 (6H, m), 3.28 (3H, s), 3.34-3.48 (2H, m), 3.55 (3H, s), 3.65-4.00 (2H, m), 4.30 (2H, d, J=7Hz), 4.62 (1H, br t, J=7Hz), 6.51 (1H, d, J=7Hz), 6.57-6.64 (2H, m), 6.76-6.95 (5H, m), 7.61-7.68 (2H, m)

Example 69

[0383] To an ice bath cooled solution of 4-(2-dimethylamino-4-methyl)phenoxymethyl-N-[2-(5-ethoxycarbonylpent-1-yl)oxy]phenylbenzamide (860 mg) in N,N-dimethylformamide (15 ml) was added sodium hydride (60% in oil, 71 mg) and the solution was stirred at the same temperature for 30 minutes. Iodomethane (0.121 ml) was added to the solution and the mixture was stirred at ambient temperature for 3 hours. The mixture was diluted with ethyl acetate (50 ml) and the solution was washed with water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give a crude oil. The crude product was purified by silica gel column chromatography (1% methanol in chloroform) to give 4-(2-dimethylamino-4-methyl)-phenoxymethyl-N-[2-(5-ethoxycarbonylpent-1-yl)oxy] phenyl-N-methylbenzamide (632 mg).

NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 1.42-1.55 (2H, m), 1.63-1.74 (2H, m), 1.76-1.87 (2H, m), 2.20 (3H, s), 2.23 (3H, s), 2.33 (2H, t, J=7.5Hz), 2.72 (6H, s), 3.30 (3H, s), 3.76-3.97 (2H, m), 4.12 (2H, q, J=7.5Hz), 5.02 (2H, s), 6.52-6.60 (3H, m), 6.70 (1H, d, J=7Hz), 6.80-6.88 (2H, m), 7.20 (2H, d, J=8Hz), 7.31 (2H, d, J=8Hz)

Example 70

[0384] The following compound was obtained by using 3-methoxy-4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-[2-(4-aminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide as a starting compound according to a similar manner to that of Example 14.

3-Methoxy-4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-[2-(4-acetylaminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.65-1.82 (4H, m), 1.76 (3H, s), 2.05 (3H, s), 2.07-2.21 (2H, m), 2.26 (3H, s), 3.22-3.38 (2H, m), 3.38 (3H, s), 3.77 (3H, s), 3.77-3.96 (2H, m), 4.24 (2H, t, J=7.5Hz), 6.53-6.71 (2H, m), 6.93-7.14 (5H, m), 7.25 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.43 (7H, d, J=7Hz)

Example 71

[0385] To a mixture of 3-methoxy-4-[2-[3-(tert-butoxycarbonyl)-aminoprop-1-yl]oxybenzoyl]amino-N-[2- (4-aminobut-1-yl)oxy-4-methyl]phenyl-N-methylbenzamide (365 mg) and N-(tert-butoxycarbonyl)glycine (111 mg) in N,N-dimethylformamide (15 ml) were added N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride (132 mg) and hydroxybenzotriazole (93.2 mg) and the mixture was stirred at ambient temperature overnight. The solution was diluted with ethyl acetate (30 ml) and the solution was washed successively with saturated aqueous sodium hydrogen carbonate, water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an amorphous. The crude product was purified by silica gel column chromatography (1% methanol in chloroform) to give 3-methoxy-4-[2-[3-tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-N-[2-4-(tert-butoxycarbonylamino)acetylaminobut-l-yl]oxy-4-methyl]phenyl-N-methylbenzamide (320 mg).

NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.42 (9H, s), 1.58-1.70 (2H, m), 1.70-1.80 (2H, m), 2.05-2.17 (2H, m), 2.27 (3H, s), 3.20-3.34 (4H, m), 3.30 (3H, s), 3.70-3.95 (4H, m), 3.74 (3H, s), 4.22 (2H, t, J=7.5Hz), 6.56-6.68 (2H, m), 6.88-7.11 (5H, m), 7.45 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz), 8.28 (1H, d, J=7Hz)

Example 72

[0386] The following compounds were obtained according to a similar manner to that of Example 71.

1) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[4-[3-(tert-butoxycarbonyl)-aminopropionylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.41 (9H, s), 1.60-1.82 (4H, m), 2.10-2.19 (2H, m), 2.29 (3H, s), 2.48 (2H, br), 3.25-3.42 (6H, m), 3.32 (3H, s), 3.79 (3H, s), 3.80-3.97 (2H, m), 4.25 (2H, t, J=5Hz), 6.59 (1H, s), 6.67 (1H, d, J=8Hz), 6.94-7.11 (5H, m), 7.45 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

2) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[4-[[1-(tert-butoxycarbonyl)-piperidin-4-yl]carbonylamino]but-1-yl]oxy-4-methylphenyl]-4-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.44 (9H, s), 1.60-1.81 (8H, m), 2.08-2.18 (2H, m), 2.29 (3H, s), 2.70 (1H, br), 3.30 (2H, q, J=5Hz), 3.32 (3H, s), 3.76 (3H, s), 3.76-4.15 (6H, m), 4.22 (2H, t, J=5Hz), 6.59 (1H, s), 6.65 (1H, d, J=8Hz), 6.94-7.10 (6H, m), 7.44 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.39 (1H, d, J=8Hz)

Example 73

[0387] To an ice-cooled mixture of 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-(4-aminobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide (430 mg) and triethylamine (68 mg) in dichloromethane (10 ml) was added phenyl chlorocarbonate (106 mg) dropwise and the solution was stirred at the same temperature for 30 minutes. The resulting mixture was diluted with dichloromethane (10 ml) and the solution was washed successively with 1N hydrochloric acid saturated aqueous sodium hydrogen carbonate and brine. The solvent was dried over magnesium sulfate and removed under reduced pressure to give 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl] amino-3-methoxy-N-[(2-(4-phenoxycarbonylaminobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide (471 mg) .
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.60-1.90 (4H, m), 2.08-2.17 (2H, m), 2.29 (3H, s), 3.27 (2H, q, J=5Hz), 3.31 (2H, t, J=5Hz), 3.36 (3H, s), 3.78 (3H, s), 3.82-4.00 (2H, m), 4.21 (2H, t, J=5Hz), 4.73 (1H, br), 5.38 (1H, br), 6.61-6.68 (2H, m), 6.91-6.99 (4H, m), 7.06-7.20 (5H, m), 7.30-7.38 (2H, m), 7.42 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=6Hz), 8.40 (1H, d, J=8Hz)

Example 74

[0388] A mixture of 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N- [2- (4-aminobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide (120 mg) and 3-(dimethylamino)prop-1-yl phenyl carbonate (127 mg) in N,N-dimethylformamide (5 ml) was stirred at 50°C for 8 hours. The reaction mixture was diluted with ethyl acetate (15 ml) and the solution was washed successively with saturated aqueous sodium bicarbonate solution and brine. The solution was dried over potassium carbonate. The solvent was evaporated and the residue was purified on silica gel column chromatography (SiO_2 20 g, 3-15% methanol in chloroform) to give 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-(3-dimethylaminoprop-1-yl)oxycarbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide (64 mg) .
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.62-1.87 (6H, m), 2.05-2.18 (2H, m), 2.28 (3H, s), 2.30 (6H, s), 2.44 (2H, t, J=5Hz), 3.20-3.32 (4H, m), 3.32 (3H, s), 3.78 (3H, s), 3.80-4.00 (2H, m), 4.12 (2H, t, J=5Hz), 4.24 (2H, t, J=5Hz), 6.59-6.64 (2H, m), 6.88-7.12 (5H, m), 7.44 (1H, dd, J=2, 8Hz), 8.21 (1H, d, J=8Hz), 8.40 (1H, br)

Example 75

[0389] To a solution of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-oxopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]-benzamide (192 mg) in methanol (5 ml) was added sodium borohydride (19 mg) at ambient temperature and the mixture was stirred at the same temperate for 1 hour. The reaction was quenched with 0.5N hydrochloric acid (10 ml) and the mixture was extracted with chloroform (15 ml x 3). The organic layer was washed with aqueous sodium hydrogen carbonate and brine, and the solution was dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[2-[5-(4-hydroxypiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide (199 mg).
NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.41-1.99 (10H, m), 2.05-2.20 (2H, m), 2.27 (3H, s), 2.30-2.51 (2H, m), 3.01-3.22 (2H, m), 3.30 (3H, s), 3.65-4.14 (7H, m), 3.76 (3H, s), 4.22 (2H, t, J=5Hz), 6.52-6.67 (2H, m), 6.78-7.10 (5H, m), 7.38-7.47 (1H, m), 8.19 (1H, d, J=7Hz), 8.39 (1H, d, J=7Hz)

Example 76

[0390] To a mixture of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-oxopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]-benzamide (250 mg), ammonium acetate (51 mg) and acetic acid (0.5 ml) in methanol (10 ml) was added sodium cyanoborohydride (21 mg) at 0°C and the mixture was stirred at ambient temperature for 12 hours. The mixture was poured into ice-cooled 1N aqueous sodium hydroxide solution

(15 ml) and the solution was extracted with chloroform (15 ml x 3). The organic layer was washed with brine and dried over potassium carbonate. The solvent was evaporated in vacuo and the residue was purified by silica gel column chromatography (SiO_2 40 g, 5-15% methanol in chloroform) to give 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy] benzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-aminopiperidin-1-yl)carbonylpent-l-yl]oxy-4-methylphenyl]benzamide (91 mg).

NMR ($CDCl_3$, δ) : 1.41 (9H, s), 1.45-2.01 (12H, m), 2.09-2.20 (2H, m), 2.28 (3H, s), 2.23-2.45 (4H, m), 2.56-2.71 (1H, br), 2.93-3.12 (2H, m), 3.25-3.36 (2H, m), 3.32 (3H, s), 3.79 (3H, s), 3.81-4.02 (2H, m), 4.23 (2H, t, J=5Hz), 4.91-4.08 (1H, br), 6.56-6.68 (2H, m), 6.82-7.13 (5H, m), 7.45 (2H, d, J=8Hz), 8.20 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

Example 77

[0391] The following compound was obtained according to a similar manner to that of Example 76.

4-[2-(3-tert-Butoxycarbonylaminoprop-l-yl)oxybenzoyl]-amino-3-methoxy-N-methyl-N-[2-[6-(4-methylpiperazin-1-yl)hex-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.45-1.84 (8H, m), 2.09-2.22 (2H, m), 2.27 (3H, s), 2.28 (3H, s), 2.32-2.59 (8H, m), 3.32 (1H, q, J=5Hz), 3.34 (3H, s), 3.80 (3H, s), 3.82-4.01 (2H, m), 4.28 (2H, t, J=5Hz), 6.56-6.65 (2H, m), 6.82-7.12 (6H, m), 7.43-7.50 (1H, m), 8.20 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

Example 78

[0392] To a mixture of 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-carboxypent-1-yl]oxy-4-methylphenyl]benzamide (250 mg), 2-dimethylaminoethanol (99 mg) and 4-dimethylaminopyridine (36 mg) in dichloromethane (10 ml) was added N-ethyl-N'-(3-dimethylaminoprop-1-yl)carbodiimide hydrochloride (71 mg) at 0°C and stirred at the same temperature for 7 hours. The mixture was diluted with chloroform (20 ml) and the solution was washed with water (20 ml x 2) and brine. The solution was dried over magnesium sulfate and the solvent was removed under reduced pressure. This residue was purified by silica gel column chromatography (SiO_2 30 g, 1-10% methanol in chloroform) to give 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2-dimethylaminoeth-1-yl)oxycarbonylpent-1-yl]oxy-4-methylpheyl]-benzamide (238 mg).

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.57 (2H, m), 1.65-1.90 (4H, m), 2.10-2.21 (2H, m), 2.28 (9H, s), 2.39 (2H, t, J=5Hz), 2.55 (2H, t, J=5Hz), 3.30 (2H, t, J=5Hz), 3.32 (3H, s), 3.79 (3H, s), 3.82-4.00 (2H, m), 4.18 (2H, t, J=5Hz), 4.24 (2H, t, J=5Hz), 4.75-4.86 (1H, br), 6.54-6.67 (2H, m), 6.81-7.11 (5H, m), 7.41-7.49 (1H, m), 8.20 (1H, d, J=8Hz), 8.49 (1H, d, J=8Hz)

Example 79

[0393] To a solution of 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-ethoxycarbonylpent-1-yl)oxy-4-methylphenyl]benzamide (400 mg) in tetrahydrofuran (5 ml) was added lithium aluminum hydride (12 mg) at -23°C and the mixture was stirred at 0°C for 3 hours. The reaction was quenched with slow addition of 0.5N hydrochloric acid (15 ml) and the solution was stirred at ambient temperature for 20 minutes. The solution was extracted with chloroform (15 ml x 3) and the organic layer was washed with aqueous saturated sodium bicarbonate solution and brine. The solution was dried over magnesium sulfate and the solvent was removed under reduced pressure to give 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N- [2-(6-hydroxyhex-1-yl)oxy-4-methylphenyl]benzamide (456 mg).

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-2.20 (10H, m), 2.27 (3H, s), 3.30 (2H, q, J=5Hz), 3.32 (3H, s), 3.64 (2H, t, J=5Hz), 3.78 (3H, s), 3.81-4.02 (2H, m), 4.23 (2H, t, J=5Hz), 6.57-6.63 (2H, m), 6.84-7.13 (6H, m), 7.41-7.49 (1H, m), 8.20 (1H, d, J=7Hz) 8.41 (1H, d, J=7Hz)

Example 80

[0394] To a solution of oxalyl chloride (95 mg) in dichloromethane (10 ml) was added dimethyl sulfoxide (117 mg) dropwise at -78°C. The mixture was warmed to -15°C and a solution of 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl) oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(6-hydroxyhex-1-yl)oxy-4-methylphenyl]benzamide (450 mg) in dichloromethane (10 ml) was added thereto. After being stirred at the same temperature for 10 minutes, to the reaction mixture was added triethylamine (343 mg) and stirred at the same temperature for 5 minutes. The resulting solution was warmed to ambient temperature and poured into water. The mixture was extracted with chloroform (15 ml x 3) and the organic layer was washed with brine. The solution was dried over magnesium sulfate and the solvent was evaporated to give 4-[2-(3-tert-butoxycarbonylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-formylpent-1-yl)oxy-4-methylphenyl]benzamide (546 mg)

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.50-1.91 (6H, m), 2.11-2.23 (2H, m), 2.27 (3H, s), 2.50 (2H, t, J=5Hz), 3.31 (1H, q, J=5Hz), 3.34 (3H, s), 3.79 (3H, s), 3.85-4.00 (2H, m), 4.27 (2H, t, J=5Hz), 6.60-6.68 (2H, m), 6.81-7.12 (6H, m), 7.42-7.51 (1H, m), 8.21 (1H, d, J=7Hz), 8.41 (1H, d, J=7Hz), 9.89 (1H, s)

Example 81

[0395] To a solution of 4-[2-[3-(tert-butoxycarbonyl)aminoprop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-(4-cyanophenylmethyl)-oxy-4-methylphenyl]-N-methylbenzamide (360 mg) in xylene (8 ml) was added trimethyltin azide (218 mg) and the solution was stirred at 120°C for 3 days. The solution was cooled to ambient temperature and 12N hydrochloric acid (10 ml) was added to the solution to decompose tin salt of the tetrazole compound and the excess reagent. Then the solution was adjusted to pH 7 with saturated aqueous sodium hydroxide at 0°C, and the solution was extracted with ethyl acetate (50 ml x 3). The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was evaporated to give a crude product. The crude product was purified by silica gel column chromatography (SiO_2 30 g, 2-25% methanol in chloroform) to give 4-[2-(3-aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(tetrazol-5-yl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide (227 mg).

NMR ($CDCl_3$, δ) : 2.15 (3H, br s), 2.14-2.26 (2H, m), 3.17 (2H, q, J=5Hz), 3.40 (3H, s), 3.57 (3H, s), 4.20 (2H, t, J=5Hz), 4.95 (1H, d, J=12Hz), 5.22 (1H, d, J=12Hz), 6.55-6.64 (2H, m), 6.80 (1H, s), 6.92-7.08 (6H, m), 7.23 (1H, br), 7.43 (1H, dd, J=2, 8Hz), 7.78 (2H, d, J=8Hz), 8.20 (1H, d, J=8Hz)

Example 82

[0396] A mixture of 4-[2-(3-aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide (275 mg) and O-methylisourea (44 mg) in ethanol (5 ml) was refluxed for 3 days. The solvent was evaporated in vacuo and the residue was purified on basic silica gel column chromatography (SiO_2 17 g, 1-80% methanol in chloroform) to give 4-[2-(3-guanidinoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide (53 mg) .

NMR ($CDCl_3$, δ) : 1.40-1.97 (6H, m), 2.06-2.20 (2H, m), 2.27 (6H, s), 2.28 (3H, s), 2.29-2.41 (4H, m), 2.50 (1H, br), 3.04 (2H, br), 3.30 (3H, s), 3.42 (2H, br), 3.76 (3H, s), 3.78 (2H, br), 3.82-4.01 (2H, m), 4.25 (2H, br), 6.55-6.68 (2H, m), 6.81-7.09 (5H, m), 7.28 (1H, s), 7.42 (1H, dd, J=2, 8Hz), 7.99 (1H, d, J=8Hz), 8.29 (1H, br)

Example 83

[0397] The following compound was obtained according to a similar manner to that of Example 6.

4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-(4-aminobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.81-1.99 (4H, m), 2.05-2.14 (2H, m), 2.24 (3H, s), 3.08 (2H, br), 3.29 (2H, br), 3.30 (3H, s), 3.70 (3H, s), 3.76-3.96 (2H, m), 4.14 (2H, t, J=5Hz), 5.07 (1H, br), 6.54-6.61 (2H, m), 6.85-7.04 (4H, m), 7.25 (1H, s), 7.37 (1H, dd, J=2, 8Hz), 8.14 (1H, d, J=8Hz), 8.38 (1H, d, J=8Hz)

Example 84

[0398] To a solution of 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yloxy]benzoylamino]-3-methoxy-N-[2-[4-(phenoxycarbonylamino)but-1-yl]-4-methylphenyl]-N-methylbenzamide (200 mg) in N,N-dimethylformamide (5 ml) was added 1-methylpiperazine (88 μl) and the solution was stirred at 80°C for 7 hours. The solution was diluted with ethyl acetate (15 ml) and washed successively with water (20 ml x 4) and brine. The solvent was dried over magnesium sulfate and removed under reduced pressure. The crude product was purified on silica gel column chromatography (SiO_2 25 g, chloroform-methanol 2-10%) to give pure 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yl]oxybenzoyl]amino-3-methoxy-N-[2-[4-[(4-methylpiperazin-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide (124 mg) .

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.60-1.81 (4H, m), 2.13-2.22 (2H, m), 2.29 (6H, s), 2.39 (4H, br), 3.79 (3H, s), 3.25-3.51 (8H, m), 3.32 (3H, s), 3.75-3.99 (2H, m), 4.26 (2H, t, J=5Hz), 6.57-6.71 (2H, m), 6.92-7.18 (6H, m), 7.48 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

Example 85

[0399] The following compounds were obtained according to a similar manner to that of Example 84.

1) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-[4-[(4-dimethylaminopiperid-

in-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.65-1.90 (4H, m), 2.29 (3H, s), 2.30 (6H, s), 2.77 (1H, t, J=11Hz), 3.29 (2H, q, J=5Hz), 3.32 (3H, s), 3.78 (3H, s), 3.85-4.11 (6H, m), 4.25 (2H, t, J=5Hz), 6.55-6.70 (2H, m), 6.92-7.13 (5H, m), 7.45 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

2) 4-[2-[3-(tert-Butoxycarbonylamino)prop-1-yl]oxybenzoyl]-amino-3-methoxy-N-[2-(4-ureidobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide
NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.45-1.80 (4H, m), 2.01-2.11 (2H, m), 2.27 (3H, s), 3.22-3.31 (2H, m), 3.30 (3H, s), 3.65-3.77 (2H, m), 3.71 (3H, s), 4.22 (2H, t, J=5Hz), 5.16 (2H, br), 6.48 (1H, s), 6.71 (1H, d, J=8Hz), 6.90-7.15 (5H, m), 7.41 (1H, dd, J=2, 8Hz), 8.11 (1H, d, J=8Hz), 8.35 (1H, d, J=8Hz)

Example 86

[0400] To a solution of 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yloxy]benzoylamino]-3-methoxy-N-[2-[4-(phenoxycarbonylamino)but-1-yl]-4-methylphenyl]-N-methylbenzamide (150 mg) in N,N-dimethylformamide (5 ml) was added dimethylamine hydrochloride (40 mg) and the mixture was stirred at 80°C for 7 hours. The mixture was cooled to ambient temperature and diluted with ethyl acetate (15 ml). The solution was washed with water (15 ml x 5) and brine, and dried over magnesium sulfate. The solvent was removed in vacuo and the residue was purified on silica gel column chromatography (SiO_2 20 g, chloroform-methanol 1-5%) to give 4-[2-[3-(tert-butoxycarbonylamino)prop-1-yloxy]benzoylamino]-3-methoxy-N-[2-[4-(N,N-dimethylureido)but-1-yloxy]-4-methylphenyl]-N-methylbenzamide (115 mg) .

NMR ($CDCl_3$, δ) : 1.40 (9H, s), 1.60-1.87 (4H, m), 2.06-2.18 (2H, m), 2.28 (3H, s), 2.90 (6H, s), 3.30 (2H, q, J=5Hz), 3.34 (3H, s), 3.79 (3H, s), 3.85-4.02. (2H, m), 4.23 (2H, t, J=5Hz), 6.57-6.64 (2H, m), 6.90-7.10 (5H, m), 7.44 (1H, dd, J=2, 8Hz), 8.20 (1H, d, J=8Hz), 8.41 (1H, d, J=8Hz)

Example 87

[0401] To a solution of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-carboxymethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-benzamide (128 mg) in methanol (5 ml) was added dropwise trimethylsilyldiazomethane (5 ml, 2.0M n-hexane solution) and stirred at ambient temperature for 30 minutes. The solution was concentrated in vacuo and the residue was purified by preparative thin layer silica gel chromatography (chloroform:methanol:28% aqueous ammonia solution, 50:5:1) to give 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methoxycarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-benzamide (85 mg).

NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.45-1.37 (8H, m), 2.00-2.10 (2H, m), 2.26 (3H, s), 2.29 (3H, s), 2.30-2.42 (6H, m), 3.18-3.27 (2H, m), 3.30 (3H, s), 3.45-3.51 (2H, m), 3.63 (2H, br), 3.79 (3H, s), 3.87-3.96 (2H, m), 4.22-4.29 (2H, m), 4.54 (2H, s), 6.53-6.13 (2H, m), 6.77-6.85 (1H, m), 6.89 (1H, br), 6.92-7.02 (2H, m), 7.02-7.10 (1H, m), 7.43-7.47 (1H, m), 8.14-8.19 (1H, m), 8.40-8.45 (1H, m)

Example 88

[0402] The following compound was obtained according to a similar manner to that of Example 8.

4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-dimethylaminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-benzamide

NMR ($CDCl_3$, δ) : 1.39 (9H, s), 1.48-1.58 (2H, m), 1.63-1.88 (6H, m), 1.97-2.09 (2H, m), 2.28 (3H, s), 2.30 (3H, s), 2.31-2.42 (6H, m), 2.99 (3H, s), 3.02 (3H, s), 3.17-3.27 (2H, m), 3.32 (3H, s), 3.50 (2H, br), 3.63 (2H, br), 3.83-3.97 (2H, m), 4.22-4.29 (2H, m), 4.67 (2H, s), 6.53-6.63 (2H, m), 6.80-6.90 (2H, m), 6.96-7.09 (3H, m), 7.93 (1H, t, J=6Hz), 8.14 (1H, d, J=6Hz), 8.38 (1H, d, J=7Hz)

Example 89

[0403] To a solution of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-ethoxycarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (102 mg) in 7.5N ammonia in methanol (5 ml) was stirred at ambient temperature for 24 hours. The solution was concentrated in vacuo to give 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-aminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide (92 mg).

NMR ($CDCl_3$, δ) : 1.37 (9H, s), 1.48-1.60 (2H, m), 1.60-1.75 (4H, m), 1.75-1.88 (2H, m), 1.97-2.08 (2H, m), 2.27 (3H, s), 2.28 (3H, s), 2.30-2.41 (6H, m), 3.17-3.27 (2H, m), 3.30 (3H, s), 3.47 (3H, s), 3.52-3.62 (2H, m), 3.90-3.97 (2H, m), 4.16-4.29 (4H, m), 5.85 (1H, br), 6.57 (1H, d, J=7Hz), 6.67 (1H, s), 6.75-6.90 (2H, m), 7.00 (1H, d, J=7Hz),

7.07-7.17 (2H, m), 8.00 (1H, s), 8.18-8.21 (1H, m), 8.25 (1H, d, J=7Hz)

Example 90

[0404] The following compound was obtained according to a similar manner to that of Example 89.

4-[2-[(3-tert-Butoxycarbonylaminoprop-1-yl)oxy]benzoyl]-amino-3-methylaminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-benzamide

NMR ($CDCl_3$, δ) : 3.37 (9H, s), 1.45-1.77 (6H, m), 1.77-1.88 (2H, m), 1.96-2.08 (2H, m), 2.28 (3H, s), 2.29 (3H, s), 2.29-2.40 (6H, m), 2.82-2.83 (3H, s), 3.18-3.27 (2H, m), 3.30 (3H, s), 3.43-3.50 (3H, m), 3.57 (2H, br), 3.90-3.97 (2H, m), 4.18-4.30 (3H, m), 6.57 (1H, d, J=6Hz), 6.65 (1H, s), 6.76-6.83 (2H, m), 7.00 (1H, d, J=7Hz), 7.06-7.15 (2H, m), 7.45 (1H, t, J=7Hz), 8.16-8.22 (2H, m)

Example 91

[0405] The following compound was obtained according to similar manners to those of Examples 8 and 16.

4-(2-Aminobenzoyl)amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl] benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.35-1.66 (4H, m), 1.66-1.82 (2H, m), 2.22 (3H, s), 2.40 (2H, t, J=7Hz), 2.73 (3H, s), 2.77-3.11 (3H, m), 3.17 (3H, s), 3.28-3.56 (3H, m), 3.76-4.17 (3H, m), 4.35-4.52 (1H, m), 6.63 (1H, d, J=9Hz), 6.79 (1H, s), 6.91 (1H, dd, J=9, 9Hz), 6.98-7.11 (2H, m), 7.22 (2H, d, J=9Hz), 7.36 (1H, dd, J=9, 9Hz), 7.54 (2H, d, J=9Hz), 7.69 (1H, d, J=9Hz)

Example 92

[0406] The following compounds were obtained according to similar manners to those of Examples 6 and 16.

1) 4-[2-[(3-Aminoprop-1-yl)amino]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yloxy]phenyl]benzamide trihydrochloride

NMR (DMSO-d_6, δ) : 1.36-1.65 (4H, m), 1.66-1.92 (4H, m), 2.23 (3H, s), 2.38 (2H, t, J=7Hz), 2.68-2.77 (3H, m), 2.77-3.12 (4H, m), 3.18 (3H, s), 3.22 (2H, t, J=7Hz), 3.28-3.56 (3H, m), 3.63 (3H, s), 3.75-4.32 (4H, m), 4.42 (1H, m), 6.58-6.69 (2H, m), 6.78 (1H, d, J=8Hz), 6.83 (1H, s), 6.86-6.96 (2H, m), 7.03 (1H, d, J=8Hz), 7.34 (1H, dd, J=8, 8Hz), 7.61 (1H, d, J=8Hz), 7.67 (1H, d, J=8Hz), 7.91-8.17 (3H, m), 9.23 (1H, s)

2) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.34-1.66 (4H, m), 1.66-1.83 (2H, m), 2.04-2.24 (2H, m), 2.32-2.46 (2H, m), 2.74 (3H, s), 2.79-3.12 (4H, m), 3.22 (3H, s), 3.29-3.58 (3H, m), 3.63-4.19 (7H, m), 4.28-4.52 (3H, m), 6.80-7.08 (4H, m), 7.08-7.36 (4H, m), 7.58 (1H, dd, J=9, 9Hz), 8.02 (1H, d, J=9Hz), 8.13 (2H, br s), 8.28 (1H, d, J=9Hz)

3) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)-carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.28-1.82 (8H, m), 1.90-2.51 (11H, m), 2.64 (6H, s), 2.74-3.06 (3H, m), 3.18 (3H, s), 3.22-4.08 (6H, m), 4.29-4.41 (2H, m), 4.51 (1H, m), 6.64 (1H, d, J=8Hz), 6.75-7.20 (5H, m), 7.27 (1H, d, J=8Hz), 7.58 (1H, m), 7.94-8.32 (5H, m)

4) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-2-chloro-N-methyl-N-[2-[5-(4-methylpiperazin-1-ylcarbonyl)pent-1-yloxy]phenyl]benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.35-1.68 (4H, m), 1.69-1.90 (2H, m), 1.92-2.12 (2H, m), 2.31-2.50 (2H, m), 2.73 (3H, br s), 2.79-3.10 (4H, m), 3.17-3.61 (7H, m), 3.92-4.26 (5H, m), 4.42 (1H, m), 6.77 (1H, m), 6.92-7.23 (6H, m), 7.34-7.58 (3H, m), 7.81 (1H, s), 7.90-8.14 (3H, m)

5) 4-[2-(3-Aminoprop-1-yl)oxy-5-methylbenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride

NMR ($CDCl_3$, δ) : 1.50-1.93 (8H, m), 2.28 (3H, s), 2.28-2.36 (2H, m), 2.31 (3H, s), 2.79 (3H, s), 3.09-3.20 (2H, m), 3.29 (3H, s), 3.80 (3H, s), 3.85-4.04 (2H, m), 4.18-4.28 (2H, m), 6.57-6.66 (2H, m), 6.80-6.95 (4H, m), 7.20-7.25 (1H, m), 7.72 (1H, br), 8.51 (1H, br)

6) 4-[2-(3-Aminoprop-1-yl)oxy-4-chlorobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carb-

onylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.45-1.86 (8H, m), 2.23 (3H, s), 2.29-2.43 (2H, m), 2.78 (3H, s), 3.05-3.16 (2H, m), 3.23 (3H, s), 3.78 (3H, s), 3.82-4.03 (2H, m), 4.18-4.32 (2H, m), 6.54-6.64 (2H, m), 6.78-7.08 (4H, m), 7.94 (1H, d, J=8Hz), 8.58 (1H, br)

7) 4-[2-(3-Aminoprop-1-yl)oxy-4-methoxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)-carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.40-1.89 (6H, m), 2.28 (3H, s), 2.30-2.61 (6H, m), 2.70-3.04 (4H, m), 3.08-3.25 (2H, m), 3.28 (3H, s), 3.80 (6H, s), 3.82-4.08 (2H, m), 4.26 (2H, br), 6.49-6.66 (4H, m), 6.78-7.00 (3H, m), 7.93-8.02 (1H, m), 8.30 (1H, br), 8.52 (2H, br)

8) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR ($DMSO-d_6$, δ) : 1.42 (2H, br), 1.53 (2H, br), 1.74 (2H, br), 2.03 (2H, br), 2.13-2.20 (2H, m), 2.30-2.38 (2H, m), 2.66 (3H, s), 2.67 (3H, s), 2.94 (4H, br), 3.20 (3H, s), 3.28-3.40 (2H, m), 3.73 (3H, s), 3.82-4.08 (4H, m), 4.33-4.40 (2H, m), 4.47-4.57 (1H, m), 6.82-7.00 (4H, m), 7.10-7.29 (4H, m), 7.53-7.60 (1H, m), 8.00 (1H, d, J=7Hz), 8.22-8.30 (1H, m)

9) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methyl-N-methyl-N- [2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR ($DMSO-d_6$, δ) : 1.40-1.53 (2H, m), 1.53-1.65 (2H, m), 1.66-1.82 (2H, m), 2.01-2.13 (2H, m), 2.18 (3H, s), 2.23 (3H, s), 2.36-2.46 (2H, m), 2.73-2.74 (3H, s), 2.78-3.08 (6H, m), 3.18 (3H, s), 4.27 (2H, br), 4.40-4.50 (1H, m), 6.65 (1H, d, J=6Hz), 6.82 (1H, s), 6.98-7.13 (3H, m), 7.17-7.30 (2H, m),7.45-7.57 (2H, m), 7.22 (1H, d, J=6Hz), 9.67 (1H, s)

10) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-ethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR ($DMSO-d_6$, δ) : 1.23 (3H, t, J=6Hz), 1.38-1.50 (2H, m), 1.50-1.65 (2H, m), 1.65-1.82 (2H, m), 2.05-2.17 (2H, m), 2.21 (3H, s), 2.32-2.43 (2H, m), 2.70-2.73 (3H, m), 2.80-3.08 (7H, m), 3.18 (3H, s), 3.22-3.55 (6H, m), 3.92-4.15 (2H, m), 4.32-4.48 (4H, m), 6.63 (1H, d, J=7Hz), 6.83 (1H, s), 6.89-6.92 (2H, m), 7.02 (1H, d, J=7Hz), 7.13 (1H, t, J=6Hz), 7.29 (1H, d, J=7Hz), 7.58 (1H, t, J=7Hz), 7.99 (1H, d, J=7Hz), 8.18-8.27 (1H, m)

Example 93

[0407] The following compounds were obtained according to similar manners to those of Examples 1 and 16.

1) 4-[2-(Dimethylamino)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR ($DMSO-d_6$, δ) : 1.36-1.65 (4H, m), 1.67-1.82 (2H, m), 2.22 (3H, s), 2.38 (2H, t, J=7Hz), 2.64-3.14 (12H, m), 3.18 (3H, s), 3.28-3.42 (2H, m), 3.50 (1H, m), 3.73 (3H, s), 3.79-4.14 (3H, m), 4.42 (1H, m), 6.64 (1H, d, J=8Hz), 6.82 (1H, s), 6.83-6.97 (2H, m), 7.02 (1H, d, J=8Hz), 7.35 (1H, m), 7.52-7.67 (2H, m), 8.07 (1H, d, J=8Hz), 8.14 (1H, m)

2) 4-[2-(Dimethylaminosulfonyl)benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yloxy]phenyl]benzamide hydrochloride
NMR ($DMSO-d_6$, δ) : 1.38-1.64 (4H, m), 1.67-1.82 (2H, m), 2.23 (3H, s), 2.38 (2H, t, J=7Hz), 2.69 (6H, s), 2.74 (3H, s), 2.80-3.12 (4H, m), 3.18 (3H, s), 3.23-3.52 (2H, m), 3.59 (3H, s), 3.81-4.16 (3H, m), 4.44 (1H, m), 6.66 (1H, d, J=9Hz), 6.77-6.96 (3H, m), 7.02 (1H, d, J=9Hz), 7.51 (1H, m), 7.60-7.92 (4H, m)

3) 3-Methoxy-4-[2-(morpholinosulfonyl)benzoyl]amino-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride
NMR ($DMSO-d_6$, δ) : 1.37-1.65 (4H, m), 1.66-1.83 (2H, m), 2.23 (3H, s), 2.32-2.44 (2H, m), 2.73 (3H, s), 2.81-3.10 (6H, m), 3.18 (3H, s), 3.25-3.71 (11H, m), 3.80-4.20 (3H, m), 4.42 (1H, m), 6.66 (1H, d, J=8Hz), 6.76-6.96 (3H, m), 7.02 (1H, d, J=8Hz), 7.53 (1H, d, J=8Hz), 7.62-7.93 (4H, m), 8.31 (1H, s)

4) 4-[2-(Isoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride
NMR ($DMSO-d_6$, δ) : 1.39 (6H, d, J=7Hz), 1.38-1.66 (4H, m), 1.67-1.83 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7Hz),

2.76 (3H, s), 2.82-3.11 (4H, m), 3.18 (3H, s), 3.74 (3H, s), 3.79-4.18 (5H, m), 4.36-4.52 (1H, m), 4.98 (1H, m), 6.65 (1H, d, J=8Hz), 6.73-7.17 (5H, m), 7.30 (1H, d, J=8Hz), 7.54 (1H, dd, J=8, 8Hz), 8.04 (1H, d, J=8Hz), 8.31 (1H, d, J=8Hz)

Example 94

[0408] The following compound was obtained according to similar manners to those of Examples 16 and 30.

4-[2-[2-[(3-Aminoprop-1-yl)oxy]phenyl]vinyl]-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.33-1.64 (4H, m), 1.64-1.83 (2H, m), 1.95-2.17 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=7Hz), 2.72 (3H, s), 2.78-3.10 (6H, m), 3.15 and 3.16 (total 3H, s), 3.28-3.60 (2H, m), 3.64 (3H, s), 3.80-4.20 (5H, m), 4.42 (1H, m), 6.44-7.60 (12H, m), 8.00-8.26 (2H, m)

Example 95

[0409] The following compounds were obtained according to similar manners to those of Examples 1 and 43.

1) 4-(2-Hydroxybenzoyl)amino-3-methoxy-N-[2-[4-(4-dimethylaminopiperidin-1-yl)carbonyl-4-methyl]phenylmethoxy]phenyl-N-methylbenzamide

MASS (m/z) : 637 (M+1)

2) 4-(2-Hydroxy)benzoylamino-3-methoxy-N-methyl-N-[2-[3-(4-methylpiperazin-1-yl)carbonylmethoxyprop-1-yl]oxy]-phenylbenzamide

NMR ($CDCl_3$, δ) : 2.05-2.16 (2H, m), 2.28 (3H, s), 2.33-2.40 (4H, m), 3.35 (3H, s), 3.40-3.45 (2H, m), 3.57-3.63 (2H, m), 3.69 (2H, t, J=7.5Hz), 3.78 (3H, s), 3.94-4.11 (2H, m), 4.12 (2H, s), 6.79-7.04 (7H, m), 7.18 (1H, t, J=7Hz), 7.42 (1H, t, J=7Hz), 7.50 (1H, d, J=7Hz), 8.20 (1H, d, J=7Hz), 8.81 (1H, s)

3) 4-(2-Hydroxy)benzoyl-3-methoxy-N-[2-[(E)-5-(4-dimethylaminopiperidin-1-yl)carbonyl-4-penten-1-yl]oxy-4-methyl]phenyl-N-methylbenzamide

NMR ($CDCl_3$, δ) : 1.33-1.53 (2H, m), 1.84-2.05 (4H, m), 2.27 (3H, s), 2.33 (3H, s), 2.40 (3H, s), 2.30-4.13 (11H, m), 3.32 (3H, s), 4.67 (1H, m), 6.30 (1H, d, J=15Hz), 6.55-6.66 (2H, m), 6.78-7.56 (8H, m), 8.18 (1H, m)

Example 96

[0410] The following compound was obtained according to similar manners to those of Examples 4, 16 and 45.

4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-(3-carboxyprop-1-yl)oxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.38-1.52 (2H, m), 1.52-1.65 (2H, m), 1.67-1.93 (4H, m), 2.05-2.16 (2H, m), 2.01 (3H, s), 2.29-2.43 (5H, m), 2.73 (3H, s), 3.22-3.56 (4H, m), 3.82-4.14 (5H, m), 4.30-4.47 (3H, m), 8.63 (1H, d, J=7Hz), 8.81 (1H, s), 8.88-8.92 (2H, m), 7.03 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz), 7.27 (1H, d, J=7Hz), 7.56 (1H, t, J=6Hz), 7.96 (1H, d, J=6Hz), 8.22 (1H, d, J=7Hz)

Example 97

[0411] The following compound was obtained according to similar manners to those of Preparation 4 and Example 16.

4-(2-Aminobenzyloxy)-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.35-1.64 (4H, m), 1.64-1.81 (2H, m), 2.23 (3H, s), 2.39 (2H, t, J=7Hz), 2.75 (3H, s), 2.80-3.09 (2H, m), 3.16 (3H, s), 3.27-3.50 (2H, m), 3.57 (3H, s), 3.73-4.15 (5H, m), 4.43 (1H, m), 5.08 (2H, s), 6.64 (1H, d, J=8Hz), 6.76-7.42 (9H, m)

Example 98

[0412] The following compound was obtained according to similar manners to those of Examples 14 and 16.

4-[2-(3-Acetylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide hydrochloride

NMR (DMSO-d_6, δ) : 1.36-1.50 (2H, m), 1.50-1.64 (2H, m), 1.67-1.84 (2H, m), 1.92-2.06 (2H, m), 2.22 (3H, s), 2.32-2.44 (2H, m), 2.50 (3H, s), 2.74 and 2.75 (total 3H, s), 2.81-3.08 (3H, m), 3.19 (3H, s), 3.30-3.54 (3H, m), 3.70

(3H, s), 3.79-4.16 (3H, m), 4.20-4.30 (2H, m), 6.64 (1H, d, J=8Hz), 6.81 (1H, s), 6.83-6.97 (2H, m), 7.03 (1H, d, J=8Hz), 7.12 (1H, dd, J=8, 8Hz), 7.25 (1H, d, J=8Hz), 7.51-7.61 (1H, m), 7.92-8.08 (2H, m), 8.28 (1H, d, J=8Hz)

Example 99

[0413] The following compound was obtained according to similar manners to those of Examples 15 and 26.

4-[2-(3-Dimethylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride

NMR ($CDCl_3$, δ) : 1.46-1.87 (6H, m), 2.26 (3H, s), 2.37 (2H, t, J=5Hz), 2.50 (2H, br), 2.76 (6H, s), 2.77 (6H, s), 3.02-3.30 (3H, m), 3.29 (3H, s), 3.79 (3H, s), 3.80-4.04 (2H, m), 4.33 (2H, br), 6.54-6.62 (2H, m), 6.72-7.13 (5H, m), 8.05 (1H, d, J=8Hz), 8.37 (1H, d, J=8Hz), 9.85 (1H, br)

Example 100

[0414] The following compound was obtained according to similar manners to those of Examples 8 and 45.

4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-(5-dimethylaminocarbonyl)pent-1-yloxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.51-2.19 (10H, m), 2.27 (3H, s), 2.35 (2H, t, J=6Hz), 2.92 (3H, s), 3.00 (3H, s), 3.32 (3H, s), 3.77 (3H, s), 3.80-4.08 (2H, m), 4.29 (2H, t, J=4Hz), 6.55-6.76 (2H, m), 6.83-7.20 (5H, m), 7.46 (1H, br), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

Example 101

[0415] The following compound was obtained according to similar manners to those of Examples 16 and 41.

4-(2-Aminobenzoyl)amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]-benzamide dihydrochloride

NMR (DMSO-d_6, δ) : 1.38-1.66 (4H, m), 1.68-1.83 (2H, m), 2.24 (3H, s), 2.34-2.44 (2H, m), 2.76 (3H, s), 2.80-3.09 (3H, m), 3.19 (3H, s), 3.30-3.53 (3H, m), 3.64 (3H, s), 3.80-4.51 (4H, m), 6.60-6.76 (2H, m), 6.79-6.97 (4H, m), 7.05 (1H, d, J=9Hz), 7.26 (1H, dd, J=9, 9Hz), 7.58-7.72 (2H, m), 9.19 (1H, br s)

Example 102

[0416] To a solution of 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (7.35 g) in ethanol (230 ml) was added 0.5M sulfuric acid in ethanol (22.3 ml) at 80°C. The mixture was stirred for 24 hours at ambient temperature. The precipitate was filtered through a glass funnel followed by rinsing with ethanol. The resulting white, crystalline solid was dried over air for 7 days to give 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-l-yloxy]phenyl]benzamide sulfate (5.2 g).

NMR (DMSO-d_6, δ) : 1.35-1.63 (4H, m), 1.65-1.81 (2H, m), 2.04-2.40 (14H, m), 2.96 (2H, t, J=7Hz), 3.03-4.06 (12H, m), 4.35 (2H, t, J=7Hz), 6.64 (1H, d, J=8Hz), 6.83(1H, s), 6.89 (1H, d, J=8Hz), 6.98 (1H, s), 7.02 (1H, d, J=8Hz), 7.13 (1H, dd, J=8, 8Hz), 7.26 (1H, d, J=8Hz), 7.59 (1H, dd, J=8, 8Hz), 8.01 (1H, d, J=8Hz), 8.23 (1H, d, J=8Hz)

Example 103

[0417] To a solution of 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]-amino-3-methoxy-N-methyl-N-[4-methyl-2-[5- (4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide (10.7 g) in ethanol (155 ml) was added a solution of L-(+) tartaric acid (2.43 g) in ethanol (60 ml) at 80°C. The solution was stirred at ambient temperature for 1 hour. The solvent was removed at reduced pressure and resulting solid was dissolved in distilled water (1 ℓ) and the solution was filtered through micro filter and the filtrate was lyophilized to give 4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide tartrate (5.2 g).

NMR (DMSO-d_6, δ) : 1.34-1.62 (4H, m), 1.66-1.81 (2H, m), 2.03-2.38 (14H, m), 2.96 (2H, t, J=7Hz), 3.18 (3H, s), 3.37-3.48 (4H, m), 3.74 (3H, s), 3.80-4.04 (4H, m), 4.33 (2H, t, J=7Hz), 6.64 (1H, d, J=8Hz), 6.83 (1H, s), 6.89 (1H, d, J=8Hz), 6.97 (1H, s), 7.02 (1H, d, J=8Hz), 7.13 (1H, dd, J=8, 8Hz), 7.26 (1H, d, J=8Hz), 7.58 (1H, dd, J=8, 8Hz), 8.02 (1H, d, J=8Hz), 8.25 (1H, d, J=8Hz)

Example 104

[0418] The following compounds were obtained according to similar manners to those of Examples 16 and 45.

1) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-(2-methylphenyl)benzamide hydrochloride
NMR (DMSO-d_6, δ) : 2.06-2.32 (5H, m), 2.87-3.05 (2H, m), 3.26 (3H, s), 3.72 (3H, s), 4.35 (2H, t, J=7Hz), 6.84-6.98 (2H, m), 7.08-7.36 (6H, m), 7.58 (1H, dd, J=8, 8Hz), 7.89-8.16 (4H, m), 8.26 (1H, d, J=8Hz)

2) 4-[3-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, 6) : 1.38-1.78 (12H, m), 1.98-2.07 (4H, m), 2.24 (3H, s), 2.36 (2H, t, J=8Hz), 2.43-2.54 (1H, m), 2.67 (3H, s), 2.69 (3H, s), 2.92-3.01 (2H, m), 3.19 (3H, s), 3.64 (3H, s), 3.88-4.03 (1H, m), 4.13 (2H, t, J=8Hz), 4.48-4.57 (1H, m), 6.65 (1H, d, J=8Hz), 6.82 (1H, s), 6.88-6.93 (2H, m), 7.03 (1H, d, J=8Hz), 7.17 (1H, d, J=8Hz), 7.38-7.52 (3H, m), 7.62 (1H, d, J=8Hz), 7.92-8.01 (2H, br), 9.33 (1H, s)
ESI-MASS (m/z) : 688 (M+H)

3) 4-[N-Methyl-2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-methyl-2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.32-1.65 (8H, m), 2.27 (3H, s), 2.33-2.40 (2H, m), 2.77 (3H, s), 2.86-3.02 (5H, m), 3.12 (3H, s), 3.33-3.70 (13H, m), 4.00-4.10 (1H, m), 4.40-4.50 (1H, m), 6.58-6.78 (6H, m), 6.84-7.00 (3H, m), 7.20 (1H, t, J=8Hz), 7.89-7.97 (2H, br s)
ESI-MASS (m/z) : 674

4) 4-[2-[3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-[4-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]phenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.37-1.73 (8H, m), 2.12-2.20 (2H, m), 2.37 (2H, t, J=8Hz), 2.72-2.79 (4H, m), 2.89-3.01 (4H, m), 3.29-3.40 (4H, m), 3.80 (3H, s), 3.89 (2H, t, J=8Hz), 3.98-4.04 (1H, m), 4.34-4.41 (3H, m), 6.80-6.86 (3H, m), 7.04-7.19 (4H, m), 7.29 (1H, t, J=8Hz), 7.59 (1H, t, J=8Hz), 7.95-8.06 (4H, m), 8.27 (1H, d, J=8Hz)
ESI-MASS (m/z) : 646 (M+H)

5) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylhomopiperazin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.47-1.89 (8H, m), 2.27 (3H, s), 2.30-2.46 (4H, m), 2.77-2.96 (2H, m), 3.15-3.63 (11H, m), 3.30 (3H, s), 3.76-4.04 (5H, m), 4.15-4.40 (2H, m), 6.60 (2H, br), 6.78-7.11 (5H, m), 7.43 (1H, br), 7.98-8.05 (1H, m), 8.29-8.37 (1H, m), 8.52 (2H, br)

6) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2-dimethylaminoethyl)aminocarbonyl]-pent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.38-1.87 (6H, m), 2.06-2.45 (4H, m), 2.22 (3H, s), 2.25-2.44 (2H, m), 2.76 (3H, s), 2.80 (3H, s), 3.07-3.22 (2H, m), 3.24 (3H, s), 3.54 (2H, br), 3.77-3.95 (2H, m), 3.80 (3H, s), 4.24 (2H, br), 6.57-6.62 (2H, m), 6.80-7.08 (4H, m), 7.39-7.47 (1H, m), 7.97 (1H, d, J=8Hz), 8.20-8.38 (2H, m)

7) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(2-dimethylaminoethyl)-N-methylaminocarbonyl]pent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.37-1.82 (6H, m), 2.22 (3H, s), 2.29-2.47 (4H, m), 2.85 (6H, s), 3.02 (3H, s), 3.08-3.33 (6H, m), 3.26 (3H, s), 3.58-3.95 (4H, m), 3.83 (3H, s), 4.28 (3H, br), 6.55-6.65 (2H, m), 6.82-7.06 (5H, m), 7.39-7.47 (1H, m), 8.03 (1H, d, J=8Hz), 8.33 (1H, br)

8) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(3-dimethylaminoprop-1-yl)carbamoyl]-pent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.37-1.99 (8H, m), 2.23 (3H, s), 2.25-2.44 (4H, m), 2.76 (6H, s), 3.05-3.41 (6H, m), 3.22 (3H, s), 3.78-3.94 (2H, m) , 4.22 (2H, br), 6.56 (2H, br), 6.81-7.04 (5H, m), 7.39 (1H, br), 8.00 (1H, br), 8.29 (1H, br), 8.56 (3H, br)

9) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[N-(3-dimethylaminoprop-1-yl)-N-methylcarbamoyl]pent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.33-1.99 (8H, m), 2.26 (3H, s), 2.26-2.47 (4H, m), 2.78 (6H, s), 2.96 (3H, s), 3.05-3.39 (6H, m), 3.26 (3H, s), 3.79-3.99 (2H, m), 3.78 (3H, s), 4.30 (2H, br), 6.62 (2H, m), 6.83-7.08 (5H, m), 7.45 (1H, br), 8.01 (1H, br), 8.35 (1H, br), 8.64 (2H, br)

10) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-hydroxypiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride

NMR ($CDCl_3$, δ) : 1.32-2.06 (10H, m), 2.23 (3H, s), 2.25-2.40 (4H, m), 2.99-3.07 (2H, m), 3.23 (3H, s), 3.43-4.00 (7H, m), 4.23 (2H, br), 6.52-6.63 (2H, m), 6.81-7.12 (4H, m), 7.38-7.49 (1H, m), 7.97 (1H, br), 8.30 (1H, br)

11) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-aminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.40-1.85 (12H, m), 2.24 (3H, s), 2.28-2.45 (2H), 2.87-3.11 (7H, m), 3.25 (3H, s), 3.84-4.00 (2H, m), 3.79 (3H, s), 4.25 (2H, br), 6.54-6.63 (2H, m), 6.95-7.09 (4H, m), 7.43 (1H, br), 8.04 (1H, br), 8.41 (1H, br)

12) 4-[2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)aminocarbonylpent-1-yl]oxy-4-methylphenyl]benzamide trihydrochloride
NMR ($CDCl_3$, δ) : 1.32-1.80 (6H, m), 2.04-2.15 (2H, m), 2.26 (3H, s), 2.90-3.36 (10H, m), 3.24 (3H, s), 3.76 (3H, s), 3.85-4.02 (2H, m), 4.26 (2H, br), 6.54-6.63 (2H, m), 6.75-7.09 (4H, m), 7.40-7.49 (1H, m), 8.00 (1H, d, J=8Hz), 8.39 (1H, br), 8.62 (1H, br)

13) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-[bis(2-hydroxyeth-1-yl)amino]carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.50-1.88 (6H, m), 2.05-2.54 (4H, m), 2.28 (3H, s), 3.03 (2H, br), 3.30 (3H, s), 3.41-3.69 (8H, m), 3.78 (3H, s), 3.82-4.00 (2H, m), 4.23 (2H, br), 6.59-6.69 (2H, m), 6.81-7.22 (4H, m), 7.46 (1H, br), 8.09 (1H, br), 8.38 (1H, br)

14) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2,2-dimethylhydrazino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.36-1.82 (6H, m), 2.22 (3H, s), 2.26-2.39 (4H, m), 2.88-3.11 (2H, m), 3.11 (6H, s), 3.32 (3H, s), 3.70-3.94 (2H, m), 3.77 (3H, s), 4.21 (2H, br), 6.52-6.61 (2H, m), 6.80-7.14 (5H, m), 7.42 (1H, br), 7.97 (1H, br), 8.25 (3H, br)

15) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(carbamoylmethylamino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.20-1.68 (6H, m), 2.08-2.41 (7H, m), 2.97-3.35 (5H, m), 3.29-4.27 (9H), 6.38-7.04 (6H, m), 7.90-8.29 (6H, m)

16) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(2-carbamoylethylamino)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.36-1.81 (6H, m), 2.06-2.40 (6H, m), 2.23 (3H, s), 3.13 (2H, br), 3.22 (3H, s), 3.32 (2H, br), 3.55-3.93 (2H, m), 3.78 (3H, s), 4.22 (2H, br), 6.53-6.63 (2H, m), 6.81-7.04 (5H, m), 7.39 (1H, br), 7.77 (1H, br), 7.99 (1H, br), 8.28-8.47 (3H, m)

17) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-pyridylaminocarbonyl)pent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.25-1.83 (6H, m), 2.10-2.49 (4H, m), 2.22 (3H, s), 2.90-3.37 (2H, m), 3.23 (3H, s), 3.68-3.95 (2H, m), 3.76 (3H, s), 4.21 (2H, br), 6.51-6.63 (2H, m), 6.66-7.04 (6H, m), 7.88-8.51 (7H, m)

18) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N- [2- [5-[4-(diethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.38 (6H, t, J=8Hz), 1.45-1.90 (10H, m), 1.93-2.08 (2H, m), 2.28 (3H, s), 2.30-2.48 (2H, m), 2.92-3.23 (5H, m), 3.25-3.36 (4H, m), 3.29 (3H, s), 3.69 (3H, s), 3.75-4.08 (3H, m), 4.28 (2H, br), 6.54-6.65 (2H, m), 6.81-7.08 (5H, m), 7.45 (1H, br), 7.93 (1H, br), 8.36 (1H, br)

19) 4- [2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[6-(4-methylpiperazin-1-yl)hex-1-yl]oxy-4-methylphenyl]benzamide trihydrochloride
NMR ($CDCl_3$, δ) : 1.36-1.94 (8H, m), 2.21 (3H, s), 2.25-2.42 (2H, m), 2.90-3.39 (6H, m), 3.10 (3H, s), 3.19 (3H, s), 3.58-4.04 (6H, m), 3.82 (3H, s), 4.18 (1H, br), 6.46-6.63 (2H, m), 6.74-6.98 (4H, m), 7.38 (1H, br), 7.97 (1H, br), 8.28 (1H, br), 8.45 (2H, br)

20) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-(2-pyridyl)phenylmethyl]oxy-4-methylphenyl]-N-methylbenzamide dihydrochloride
NMR ($CDCl_3$, δ) : 2.29 (3H, s), 2.39 (2H, br), 3.17 (2H, br), 3.37 (3H, s), 3.44 (3H, br), 4.12-4.30 (2H, m), 4.73 (1H, br), 5.07 (1H, br), 6.61 (1H, br), 6.70-6.79 (2H, m), 6.94-7.03 (2H, m), 7.12 (1H, d, J=8Hz), 7.38-7.47 (3H, m),

7.89-8.23 (5H, m), 8.73 (3H, br), 8.90 (1H, br)

21) 4-[2-(3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-[4-[(4-methylpiperazin-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.62-2.04 (4H, m), 2.23 (3H, s), 2.27-2.40 (2H, m), 2.74 (3H, s), 3.03-3.14 (2H, m), 3.22 (3H, s), 3.35-3.51 (4H, m), 3.78 (3H, s), 3.85-3.96 (2H, m), 4.26 (2H, br), 6.57-6.64 (2H, m), 6.67-7.09 (5H, m), 7.42 (1H, m), 7.96 (1H, d, J=8Hz), 8.30 (1H, d, J=8Hz), 8.60 (3H, br)

22) 4-[2-(3-Aminoprop-1-yl)oxybenzoylamino]-3-methoxy-N-[2-[4-[(4-dimethylaminopiperidin-1-yl)carbonylamino]but-1-yl]oxy-4-methylphenyl]-N-methylbenzamide dihydrochloride
NMR ($CDCl_3$, δ) : 1.58-2.12 (10H, m), 2.27 (3H, s), 2.30-2.48 (2H, m), 2.57-2.81 (8H, m), 3.05-3.31 (7H, m), 3.27 (3H, s), 3.75-3.99 (5H, m), 4.27 (1H, br), 6.57-6.63 (2H, m), 6.85-7.09 (5H, m), 7.44 (2H, br), 7.96 (1H, br), 8.34 (1H, br), 8.75 (1H, br)

23) 4- [2- (3-Aminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-[2-(4-ureidobut-1-yl)oxy-4-methylphenyl]-N-methylbenzamide hydrochloride
NMR ($CDCl_3$, δ) : 1.42-1.81 (4H, m), 2.00-2.15 (2H, m), 2.25 (3H, s), 2.88 (2H, t, J=5Hz), 2.92 (2H, br), 3.30 (3H, s), 3.63-3.80 (2H, m), 3.71 (3H, s), 4.21 (2H, t, J=5Hz), 6.51 (1H, s), 6.71 (1H, d, J=8Hz), 6.85-7.12 (5H, m), 7.44 (1H, dd, J=2, 8Hz), 8.12 (1H, d, J=8Hz), 8.36 (1H, d, J=8Hz)

24) 4-[2-[3-Aminoprop-1-yl)oxy]benzoyl]amino-3-chloro-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.34-1.50 (2H, m), 1.50-1.62 (2H, m), 1.65-1.80 (2H, m), 1.98-2.17 (4H, m), 2.22 (3H, s), 2.30-2.40 (2H, m), 2.66 (3H, s), 2.67 (3H, s), 2.85-3.05 (3H, m), 3.17 (3H, s), 3.33 (1H, br), 3.80-4.07 (3H, m), 4.33-4.42 (2H, m), 4.47-4.57 (1H, m), 6.68 (1H, d, J=7Hz), 6.82 (1H, s), 7.08-7.23 (3H, m), 7.29 (1H, d, J=7Hz), 7.41 (1H, s), 7.68 (1H, t, J=6Hz), 7.92 (1H, d, J=7Hz), 8.09 (1H, d, J=7Hz)

25) 3-(3-Aminoprop-1-yl)oxy-4-[2-[3-aminoprop-1-yl)oxy]-benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide trihydrochloride
NMR (DMSO-d_6, δ) : 1.37-1.50 (2H, m), 1.50-1.62 (2H, m), 1.67-1.80 (2H, m), 1.97-2.19 (4H, m), 2.22 (3H, s), 2.30-2.41 (2H, m), 2.57 (1H, s), 2.92 (6H, br), 3.17 (3H, s), 3.68 (1H, br), 3.93 (2H, br), 4.10 (2H, br), 4.40 (2H, br), 6.66 (1H, d, J=6Hz), 6.78-6.87 (2H, m), 6.95-7.04 (2H, m), 7.12 (1H, t, J=6Hz), 7.29(1H, d, J=7Hz), 7.57 (1H, t, J=6Hz), 7.93 (1H, d, J=6Hz),8.14 (1H, d, J=7Hz)

26) 2-Amino-4-[2-[(3-aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide trihydrochloride
NMR (DMSO-d_6, δ) : 1.41-1.51 (2H, m), 1.51-1.66 (1H, m), 1.74-1.84 (1H, m), 1.98-2.12 (4H, m), 2.30-2.40 (2H, m), 2.67 (3H, s), 2.68 (3H, s), 2.89-3.06 (4H, m), 3.16 (3H, s), 3.33 (2H, br), 3.96-4.10 (4H, m), 4.13-4.20 (2H, m), 4.47-4.58 (1H, m), 6.60 (1H, d, J=7Hz), 6.78 (2H, s), 6.85 (1H, s), 6.97-7.07 (2H, m), 7.13 (1H, d, J=7Hz), 7.27 (1H, s), 7.43-7.56 (2H, m)

27) 2-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5- (4-dimethylamnopiperidin-1-yl) carbonylpent-1-yloxy]-4-methylphenyl]-5-pyridinecarboxamide trihydrochloride
NMR (DMSO-d_6, δ) : 1.32-1.80 (8H, m), 1.97-2.20 (4H, m), 2.22 (3H, s), 2.27-2.40 (3H, m), 2.65 (3H, s), 2.67 (3H, s), 2.92-3.10 (4H, m), 3.19 (3H, s), 3.33 (1H, br), 3.80-4.07 (3H, m), 4.22-4.29 (2H, m), 6.69 (1H, d, J=7Hz), 6.82 (1H, s), 7.07-7.14 (2H, m), 7.20 (1H, d, J=7Hz), 7.56 (1H, t, J=6Hz), 7.66 (1H, d, J=6Hz), 7.78 (1H, d, J=7Hz), 8.00-8.04 (1H, m), 8.23 (1H, s)

28) 4-[N-[2-[(3-Aminoprop-1-yl)oxy]phenyl]amino]methyl-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl) carbonylpent-1-yloxy]-4-methylphenyl]benzamide trihydrochloride
NMR (DMSO-d_6, δ) : 1.35-1.49 (2H, m), 1.49-1.62 (2H, m), 1.62-1.79 (2H, m), 2.01-2.16 (2H, m), 2.23 (3H, s), 2.34-2.40 (2H, m), 2.71 and 2.72 (total 3H, s), 2.76-3.12 (8H, m), 3.17 (3H, s), 3.27-3.41 (2H, m), 3.41-3.54 (4H, m), 3.70-3.81 (1H, m), 3.89-3.98 (1H, m), 4.02-4.08 (3H, m), 4.25 (2H, s), 4.39-4.45 (1H, m), 6.60-6.80 (6H, m), 6.93 (2H, s), 6.98 (1H, d, J=7Hz), 7.10(1H, d, J=7Hz)

29) 4-[2-[(3-Aminoprop-1-yl)oxy]phenyl]oxymethyl-3-methoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.39-1.50 (2H, m), 1.50-1.63 (2H, m), 1.65-1.82 (2H, m), 1.97-2.10 (2H, m), 2.21 (3H, s),

2.35-2.41 (2H, m), 2.71 and 2.72 (total 3H, s), 2.78-3.10 (7H, m), 3.18 (3H, s), 3.29-3.41 (2H, m), 3.41-3.67 (4H, m), 3.82 (1H, br), 3.89-4.00 (1H, m), 4.00-4.12 (3H, m), 4.38-4.48 (1H, m), 4.57 and 4.93 (total 2H, s), 6.61 (1H, d, J=7Hz), 6.69-6.97 (6H, m), 6.97-7.07 (2H, m), 7.20-7.25 (1H, m)

30) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-benzyloxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.37-1.50 (2H, m), 1.50-1.63 (2H, m), 1.63-1.79 (2H, m), 1.79-1.91 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=6Hz), 2.60-2.77 (5H, m), 2.79-3.10 (4H, m), 3.15 (3H, s), 3.30-3.67 (3H, m), 3.77-4.12 (5H, m), 4.37-4.49 (1H, m), 5.06 (2H, s), 6.62 (1H, d, J=6Hz), 6.82 (1H, s), 6.90 (1H, d, J=7Hz), 6.97 (1H, d, J=7Hz), 7.03 (1H, s), 7.12 (1H, t, J=7Hz), 7.22 (1H, d, J=7Hz), 7.30-7.46 (5H, m), 7.54 (1H, t, J=6Hz), 7.97 (1H, d, J=7Hz), 8.23 (1H, d, J=7Hz)

31) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-hydroxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.43 (2H, br), 1.49-1.62 (2H, m), 1.63-1.82 (2H, m), 2.00-2.40 (16H, m), 2.90-2.97 (2H, m), 3.14 (3H, s), 3.30-3.50 (5H, m), 3.89 (2H, br), 4.20-4.38 (2H, m), 6.50-6.68 (2H, m), 6.80 (1H, s), 6.87-6.99 (2H, m), 7.12 (1H, t, J=6Hz), 7.22 (1H, d, J=6Hz), 7.49-7.60 (1H, m), 7.97-8.18 (2H, m)

32) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-ethoxycarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.09 and 1.22 (total 3H, t, J=6Hz), 1.37-1.51 (2H, m), 1.51-1.66 (2H, m), 1.67-1.80 (2H, m), 2.05-2.18 (2H, m), 2.23 (3H, s), 2.38 (2H, t, J=6Hz), 2.73-2.74 (3H, m), 2.90-3.10 (5H, m), 3.17 (3H, s), 3.30-3.58 (2H, m), 3.80-4.00 (2H, m), 4.00-4.20 (3H, m), 4.32-4.50 (3H, m), 4.80 (2H, s), 6.62 (1H, d, J=6Hz), 6.82 (1H, s), 6.89-6.92 (2H, m), 7.01 (1H, d, J=7Hz), 7.15 (1H, t, J=6Hz), 7.27 (1H, d, J=7Hz), 7.58 (1H, t, J=6Hz), 8.00 (1H, d, J=6Hz), 8.27 (1H, d, J=7Hz)

33) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methoxycarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.35-1.50 (2H, m), 1.50-1.63 (2H, m), 1.63-1.90 (2H, m), 2.00-2.14 (2H, m), 2.21 (3H, s), 2.25-2.43 (2H, m), 2.71 (3H, s), 2.77-3.05 (5H, m), 3.15 (3H, s), 3.18-3.57 (6H, m), 3.70 (3H, s), 3.73-4.12 (3H, m), 4.12-4.49 (3H, m), 4.80 (2H, s), 6.63 (1H, d, J=7Hz), 6.70-7.20 (5H, m), 7.27 (1H, d, J=7Hz), 7.57 (1H, t, J=7Hz), 7.93-8.10 (1H, m), 8.23 (1H, d, J=6Hz)

34) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-dimethylaminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.37-1.49 (2H, m), 1.50-1.62 (2H, m), 1.63-1.79 (2H, m), 1.98-2.10 (2H, m), 2.21 (3H, s), 2.32-2.43 (2H, m), 2.71 (3H, s), 2.86 (3H, s), 2.98 (3H, s), 2.82-3.05 (5H, m), 3.15 (3H, s), 3.90 (2H, br), 4.02-4.12 (2H, m), 4.28-4.38 (2H, m), 4.38-4.48 (1H, m), 4.83 (2H, s), 6.62 (1H, d, J=7Hz), 6.80 (1H, s), 6.82-6.92 (2H, m), 7.00 (1H, d, J=7Hz), 7.12 (1H, t, J=7Hz), 7.23 (1H, d, J=7Hz), 7.55 (1H, t, J=7Hz), 8.20 (1H, d, J=7Hz)

35) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-methylaminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.38-1.51 (1H, m), 1.51-1.65 (2H, m), 1.68-1.80 (2H, m), 2.00-2.23 (2H, m), 2.22 (3H, s), 2.34-2.40 (3H, m), 2.50 (3H, s), 2.58 (2H, br), 2.62 (3H, s), 2.63 (3H, s), 2.90 (4H, br), 3.15 (3H, s), 3.88-3.97 (2H, m), 4.26-4.33 (2H, m), 4.37-4.54 (2H, m), 6.62 (1H, d, J=7Hz), 6.82 (2H, s), 6.88 (1H, d, J=7Hz), 6.97 (1H, d, J=7Hz), 7.12 (1H, t, J=7Hz), 7.22 (1H, d, J=7Hz), 7.57 (1H, t, J=7Hz), 7.90 (1H, d, J=7Hz), 8.12-8.25 (2H, m)

36) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-aminocarbonylmethoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-l-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.38-1.52 (2H, m), 1.52-1.67 (2H, m), 1.68-1.83 (2H, m), 2.00-2.15 (2H, m), 2.23 (3H, s), 2.39 (2H, t, J=6Hz), 2.62 and 2.63 (total 3H, s), 2.72 and 2.73 (total 3H, s), 2.80-3.10 (6H, m), 3.15 (3H, s), 3.87-3.98 (2H, m), 4.03-4.13 (1H, m), 6.27-6.37 (1H, m), 6.37-6.56 (2H, m), 6.62 (1H, d, J=7Hz), 6.82 (2H, s), 6.90 (1H, d, J=7Hz), 6.98 (1H, d, J=6Hz), 7.12 (1H, t, J=7Hz), 7.26 (1H, d, J=7Hz), 7.57 (1H, t, J=6Hz), 7.92 (1H, d, J=7Hz), 8.13-8.30 (2H, m)

37) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-3-propoxybenzamide dihydrochloride
NMR (DMSO-d_6, δ) : 0.89 (3H, t, J=6Hz), 1.37-1.50 (2H, m), 1.50-1.68 (4H, m), 1.68-1.80 (2H, m), 2.02-2.18 (2H,

m), 2.20 (3H, s), 2.38 (2H, t, J=6Hz), 2.47 (3H, s), 2.75-3.12 (5H, m), 3.17 (3H, s), 3.30-3.42 (2H, m), 3.42-3.56 (1H, m), 3.80-4.00 (4H, m), 4.00-4.13 (1H, m), 4.32-4.50 (4H, m), 6.61 (1H, d, J=7Hz), 6.82 (1H, s), 6.88 (1H, s), 6.94 (1H, d, J=7Hz), 7.02 (1H, d, J=7Hz), 7.13 (1H, t, J=7Hz), 7.29 (1H, d, J=7Hz), 7.56 (1H, t, J=7Hz), 7.97 (1H, d, J=7Hz), 8.22 (1H, d, J=7Hz)

38) 4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-isopropoxy-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]benzamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.10-1.27 (6H, m), 1.37-1.50 (2H, m), 1.50-1.64 (2H, m), 1.67-1.82 (2H, m), 2.03-2.07 (2H, m), 2.22 (3H, s), 2.39 (2H, t, J=6Hz), 2.72 and 2.73 (total 3H, s), 2.78-3.12 (6H, m), 3.17 (3H, s), 3.30-3.43 (2H, m), 3.43-3.60 (1H, m), 3.80-4.02 (2H, m), 4.02-4.13 (1H, m), 4.23-4.50 (4H, m), 6.64 (1H, d, J=7Hz), 6.81-6.90 (2H, m), 6.98 (1H, d, J=7Hz), 7.03 (1H, d, J=7Hz), 7.13 (1H, t, J=6Hz), 7.32 (1H, d, J=7Hz) 7.56 (1H, t, J=6Hz), 7.94 (1H, d, J=6Hz), 8.22 (1H, d, J=7Hz)

39) 2-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-N-methyl-N-[2-[5-(4-methylpiperazin-1-yl)carbonylpent-1-yloxy]-4-methylphenyl]-5-thiophenecarboxamide dihydrochloride
NMR (DMSO-d_6, δ) : 1.20-1.38 (2H, m), 1.38-1.52 (2H, m), 1.53-1.70 (2H, m), 1.98-2.10 (2H, m), 2.22-2.32 (2H, m), 2.33 (3H, s), 2.69-2.72 (3H, m), 2.76-3.07 (5H, m), 3.16 (3H, s), 3.27-3.54 (3H, m), 3.78-4.09 (3H, m), 4.10-4.20 (2H, m), 4.33-4.47 (2H, m), 6.15 (1H, br), 6.55 (1H, d, J=5Hz), 6.81 (1H, d, J=7Hz), 6.97 (1H, s], 7.07 (1H, t, J=6Hz), 7.13-7.20 (2H, m), 7.44-7.60 (2H, m)

Example 105

[0419] To a solution of 4-[2-[(3-tert-butoxycarbonylaminoprop-1-yl)oxy]benzoyl]amino-3-methoxy-N-methyl-N-(4-hydroxyphenyl)benzamide (50 mg) in chloroform (3.0 ml) was added a solution of 4N hydrogen chloride in ethyl acetate (1.0 ml) and the mixture was stirred at ambient temperature for 2 hours. The resulting mixture was evaporated in vacuo and the residue was solidified with diethyl ether. Diethyl ether was removed in vacuo to give 4-[2-[(3-aminoprop-1-yl) oxy]benzoyl]amino-3-methoxy-N-methyl-N-(4-hydroxyphenyl)-benzamide hydrochloride (40 mg) .

NMR (DMSO-d_6, δ) : 2.11-2.21 (2H, m), 2.96 (2H, q, J=8Hz), 3.30 (3H, s), 3.78 (3H, s), 4.37 (2H, t, J=8Hz), 6.66 (2H, d, J=8Hz), 6.88 (1H, d, J=8Hz), 6.97 (1H, s), 6.99 (2H, d, J=8Hz), 7.15 (1H, t, J=8Hz), 7.27 (1H, d, J=8Hz), 7.55-7.62 (1H, m), 7.97-8.05 (3H, m), 8.28 (1H, d, J=8Hz), 9.54-9.59 (1H, br s)

ESI-MASS (m/z) : 450 (M+H)

Example 106

[0420] The following compound was obtained according to a similar manner to that of Example 105.

4-[2-[(3-Aminoprop-1-yl)oxy]benzoyl]amino-3-carboxymethoxy-N-methyl-N-cyclohexylbenzamide hydrochloride

NMR (DMSO-d_6, δ) : 1.02-1.10 (2H, m), 1.46-1.80 (8H, m), 2.08-2.12 (2H, m), 2.80 (3H, s), 2.92-2.99 (2H, m), 3.30-3.47 (2H, br), 4.39 (2H, t, J=7Hz), 4.96 (2H, s), 6.98-7.04 (2H, br s), 7.18 (1H, t, J=8Hz), 7.30 (1H, d, J=8Hz), 7.60 (1H, t, J=8Hz), 7.95-8.05 (3H, br), 8.07 (1H, d, J=8Hz), 8.51 (1H, d, J=8Hz)

ESI-MASS (m/z) : 484 (M+H)

Example 107

[0421]

1) A solution of 4-[2-[3- (9-fluorenylmethyl)oxycarbonylamininoprop-1-yl]thiobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl)carbonylpent-1-yl]oxy-4-methyiphenyl]benzamide (110 mg) in a mixture of N,N-dimethylformamide and piperidine (4:1, 5 ml) was stirred at ambient temperature for 30 minutes and the resulting solution was diluted with ethyl acetate (20 ml). The solution was washed with water (10 ml x 3) and brine, and the solution was dried over potassium carbonate. The solvent was evaporated and the residue was purified on basic silica gel column chromatography (SiO_2 30 g, 1-15% methanol in chloroform) to give 4- [2- (3-aminoprop-1-yl)thiobenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl]carbonylpent-1-yl]oxy-4-methylphenyl]benzamide.

NMR ($CDCl_3$, δ) : 1.36-1.92 (12H, m), 2.29 (6H, s), 2.30 (3H, s), 2.36 (2H, t, J=5Hz), 2.59 (1H, t, J=11Hz), 2.77 (2H, t, J=5Hz), 2.99 (2H, t, J=5Hz), 3.32 (3H, s), 3.75 (3H, s), 3.85-4.03 (4H, m), 6.57-6.66 (2H, m), 6.84-6.90 (1H, d, J=8Hz), 7.02 (1H, s), 7.39-7.48 (3H, m), 7.65 (1H, d, J=8Hz), 8.30 (1H, d, J=8Hz), 8.80 (1H, s)

2) To a solution of the obtained compound in ethanol (5 ml) was added 1N hydrochloric acid (0.15 ml). The volatile

solvent was removed by evaporation and the residue was lyophilized to give 4-[2-(3-aminoprop-1-yl)thiobenzoyl] amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl]-carbonylpent-1-yl]oxy-4-methylphenyl]benzamide dihydrochloride (45 mg).

NMR ($CDCl_3$, δ) : 1.44-1.92 (6H, m), 2.02-2.16 (2H, m), 2.28 (3H, s), 2.30-2.41 (2H, m), 2.73 (6H, br), 2.99-3.14 (2H, m), 3.27-3.33 (1H, m), 3.31 (3H, s), 3.62-3.79 (4H, m), 3.71 (3H, s), 3.82-4.10 (2H, m), 6.55-6.67 (2H, m), 6.83-7.02 (5H, m), 7.35-7.52 (2H, m), 8.23 (1H, br), 8.54 (2H, br)

Example 108

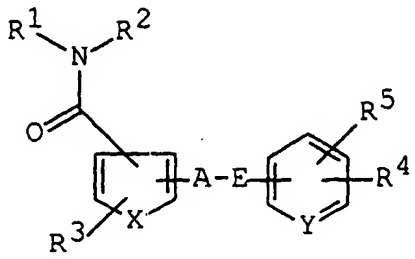
[0422] The following compound was obtained according to a similar manner to that of Example 15.

4-2-(3-Dimethylaminoprop-1-yl)oxybenzoyl]amino-3-methoxy-N-methyl-N-[2-[5-(4-dimethylaminopiperidin-1-yl) carbonylpent-1-yl]oxy-4-methylphenyl]benzamide

NMR ($CDCl_3$, δ) : 1.49-1.60 (2H, m), 1.66-1.95 (4H, m), 2.21 (6H, s), 2.27 (6H, s), 2.35-2.48 (4H, m), 2.58 (2H, t, J=11Hz), 3.32 (2H, t, J=11Hz), 3.33 (3H, s), 3.80 (3H, s), 3.82-4.00 (2H, m), 4.25 (2H, t, J=5Hz), 4.64 (1H, br), 6.55-6.64 (2H, m), 6.85 (1H, d, J=8Hz), 6.89 (1H, d, J=8Hz), 7.00-7.11 (3H, m), 7.26 (1H, s), 7.40-7.48 (1H, m), 8.21 (1H, d, J=8Hz), 8.40 (1H, d, J=8Hz)

Claims

1. A compound of the formula:



(I)

wherein

R^1 is aryl, cyclo(C_3-C_6)alkyl, pyridyl or thienyl,
each of which may be substituted with substituent(s) selected from the group consisting of halogen; hydroxy; nitro; amino; acyl; substituted acyl; acyl(C_1-C_6)alkylsulfinyl; acyl(C_1-C_6)alkylsulfonyl; acyloxy; C_1-C_6 alkylamino (C_1-C_6)alkylcarbamoyloxy; aryl; cyano; a heterocyclic group; C_2-C_6 alkenyl optionally substituted with acyl, substituted acyl, aryl or acyl-substituted aryl;
C_2-C_6 alkynyl optionally substituted with amino, acylamino or substituted acylamino;
C_1-C_6 alkyl optionally substituted with halogen, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, hydroxy, acyloxy, acyl(C_1-C_6)alkanoyloxy, acyl, substituted acyl, acyl(C_1-C_6)alkoxyimino, aryl or acyl-substituted aryl;
C_1-C_6 alkylthio optionally substituted with acyl or substituted acyl;
alkoxy optionally substituted with aryl, substituted aryl, hydroxy, acyloxy, amino, C_1-C_6 alkylamino, protected amino, a heterocyclic group, acyl-substituted pyridyl, substituted acyl-substituted pyridyl, halogen, acyl(C_1-C_6)alkylamino, N-protected-acyl(C_1-C_6)alkylamino, N-acyl(C_1-C_6)alkyl-N- C_1-C_6 alkylamino, acyl, substituted acyl, acylamino, substituted acylamino, C_1-C_6 alkylhydrazinocarbonylamino, hydroxyimino, acyl(C_1-C_6)alkoxyimino, substituted acyl(C_1-C_6)alkoxyimino, acyl(C_1-C_6)alkoxy, guanidino or N-protected guanidino; and
C_2-C_6 alkenyloxy optionally substituted with acyl or substituted acyl;

R^2 is hydrogen; C_1-C_6 alkyl optionally substituted with
hydroxy, aryl or acyl; or cyclo(C_3-C_6)alkyl;

R^3 is hydrogen; halogen; hydroxy; acyloxy; substituted
acyloxy; C_1-C_6 alkyl optionally substituted with hydroxy or C_1-C_6 alkoxy; C_1-C_6 alkoxy optionally substituted with aryl, amino, protected amino, acyl, hydroxy, cyano or C_1-C_6 alkylthio; nitro; amino; acyl; substituted acyl;

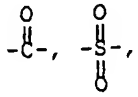
or cyclo(C_3-C_6)alkyloxy;

R^4 is hydroxy; halogen; nitro; amino; protected amino; C_1-C_6 alkylamino; acyloxy; amino(C_1-C_6)alkylamino; N-protected amino(C_1-C_6)alkylamino; C_1-C_6 alkoxy optionally substituted with hydroxy, aryl, substituted aryl, acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group or guanidino; C_1-C_6 alkylthio optionally substituted with acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, C_1-C_6 alkylsulfonyloxy, arylsulfonyloxy, ar(C_1-C_6)alkoxy or substituted ar(C_1-C_6)alkoxy; C_1-C_6 alkyl substituted with acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, C_1-C_6 alkylsulfonyloxy or arylsulfonyloxy; C_2-C_6 alkenyl optionally substituted with acyl; C_2-C_6 alkynyl optionally substituted with hydroxy, amino, protected amino, C_1-C_6 alkylsulfonyloxy or arylsulfonyloxy; amino(C_1-C_6)alkylsulfonyl; N-protected amino(C_1-C_6)alkylsulfonyl; C_1-C_6 alkylaminosulfonyl; a heterocyclicsulfonyl; amino(C_1-C_6)alkylsulfinyl; N-protected amino(C_1-C_6)alkylsulfinyl; piperidyloxy; or N-protected piperidyloxy;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy or halogen;

A is a single bond, O or NH;

E is C_1-C_6 alkylene, C_2-C_6alkenylene,



or a group of the formula :

-G-J-

in which G is C_1-C_6 alkylene and J is O or

(wherein R^6 is hydrogen or N-protective group);

X is -CH=CH-, -CH=N- or S; and

Y is CH or N;

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, wherein

R^1 is aryl which may be substituted with C_1-C_6 alkoxy optionally substituted with acylamino or acyl;
R^2 is C_1-C_6 alkyl;
R^3 is hydrogen, C_1-C_6 alkyl or C_1-C_6 alkoxy;
R^4 is hydroxy, or C_1-C_6 alkoxy or C_1-C_6 alkylthio, each of which may be substituted with hydroxy, acyl, amino, C_1-C_6 alkylamino, acylamino, protected amino or a heterocyclic group;
R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy or halogen;
A is NH;
E is

X is —CH=CH-; and
Y is CH.

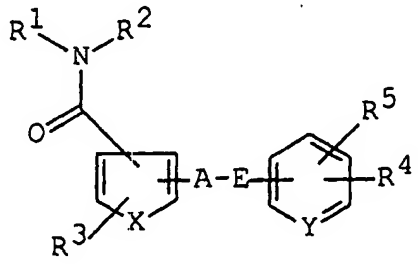
3. A compound according to claim 2, wherein

R^1 is phenyl or tolyl, each of which is substituted with C_1-C_6 alkoxy substituted with acyl;
R^3 is C_1-C_6 alkyl or C_1-C_6 alkoxy;
R^4 is C_1-C_6 alkoxy or C_1-C_6 alkylthio, each of which is substituted with amino or hydroxy.

4. A compound according to claim 3, wherein

R^1 is phenyl or tolyl, each of which is substituted with C_1-C_6 alkoxy substituted with N-(C_1-C_6)alkyl)piperazinylcarbonyl;
R^3 is C_1-C_6 alkoxy;
R^4 is C_1-C_6 alkoxy substituted with amino ; and
R^5 is hydrogen.

5. A process for preparing the formula:



(I)

wherein

R^1 is aryl, cyclo(C_3-C_6)alkyl, pyridyl or thienyl,
each of which may be substituted with substituent(s) selected from the group consisting of halogen; hydroxy; nitro; amino; acyl; substituted acyl; acyl(C_1-C_6)alkylsulfinyl; acyl(C_1-C_6)alkylsulfonyl; acyloxy; C_1-C_6 alkylamino (C_1-C_6)alkylcarbamoyloxy; aryl; cyano; a heterocyclic group;
C_2-C_6 alkenyl optionally substituted with acyl, substituted acyl, aryl or acyl-substituted aryl;
C_2-C_6 alkynyl optionally substituted with amino, acylamino or substituted acylamino;
C_1-C_6 alkyl optionally substituted with halogen, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, hydroxy, acyloxy, acyl(C_1-C_6)alkanoyloxy, acyl, substituted acyl, acyl(C_1-C_6)alkoxyimino, aryl or acyl-substituted aryl;
C_1-C_6 alkylthio optionally substituted with acyl or substituted acyl;
alkoxy optionally substituted with aryl, substituted aryl, hydroxy, acyloxy, amino, C_1-C_6 alkylamino, protected amino, a heterocyclic group, acyl-substituted pyridyl, substituted acyl-substituted pyridyl, halogen, acyl(C_1-C_6)alkylamino, N-protected-acyl(C_1-C_6)alkylamino, N-acyl(C_1-C_6)alkyl-N- C_1-C_6 alkylamino, acyl, substituted acyl, acylamino, substituted acylamino, C_1-C_6 alkylhydrazinocarbonylamino, hydroxyimino, acyl(C_1-C_6)alkoxyimino, substituted acyl(C_1-C_6)alkoxyimino, acyl(C_1-C_6)alkoxy, guanidino or N-protected guanidino; and
C_2-C_6 alkenyloxy optionally substituted with acyl or substituted acyl;

R^2 is hydrogen; C_1-C_6 alkyl optionally substituted with
hydroxy, aryl or acyl or cyclo(C_3-C_6)alkyl;

R^3 is hydrogen; halogen; hydroxy; acyloxy; substituted
acyloxy; C_1-C_6 alkyl optionally substituted with hydroxy or C_1-C_6 alkoxy; C_1-C_6 alkoxy optionally substituted with aryl, amino, protected amino, acyl, hydroxy, cyano or C_1-C_6 alkylthio; nitro; amino; acyl; substituted acyl;

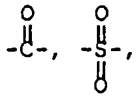
or cyclo(C_3-C_6)alkyloxy;

R^4 is hydroxy; halogen; nitro; amino; protected amino;
C_1-C_6 alkylamino; acyloxy; amino(C_1-C_6)alkylamino;
N-protected amino(C_1-C_6)alkylamino;
C_1-C_6 alkoxy optionally substituted with hydroxy, aryl, substituted aryl, acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group or guanidino; C_1-C_6 alkylthio optionally substituted with acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, C_1-C_6 alkylsulfonyloxy, arylsulfonyloxy, ar(C_1-C_6) alkoxy or substituted ar(C_1-C_6)alkoxy; C_1-C_6 alkyl substituted with acyl, substituted acyl, amino, C_1-C_6 alkylamino, acylamino, substituted acylamino, protected amino, a heterocyclic group, hydroxy, C_1-C_6 alkylsulfonyloxy or arylsulfonyloxy; C_2-C_6 alkenyl optionally substituted with acyl; C_2-C_6 alkynyl optionally substituted with hydroxy, amino, protected amino, C_1-C_6 alkylsulfonyloxy or arylsulfonyloxy;
amino(C_1-C_6)alkylsulfonyl; N-protected amino(C_1-C_6)alkylsulfonyl; C_1-C_6 alkylaminosulfonyl; a heterocyclicsulfonyl; amino(C_1-C_6)alkylsulfinyl;
N-protected amino(C_1-C_6)alkylsulfinyl; piperidyloxy; or N-protected piperidyloxy;

R^5 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy or halogen;

A is a single bond, O or NH;

E is C_1-C_6 alkylene, C_2-C_6alkenylene,



or a group of the formula :

-G-J-

in which G is C_1-C_6 alkylene and J is O or

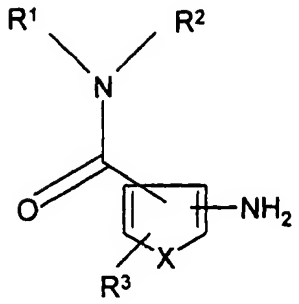
(wherein R^6 is hydrogen or N-protective group);

X is -CH=CH-, -CH=N- or S; and

Y is CH or N;

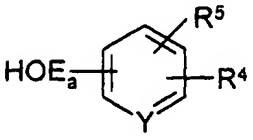
or pharmaceutically acceptable salts thereof,
which comprises,

1) reacting a compound of the formula:



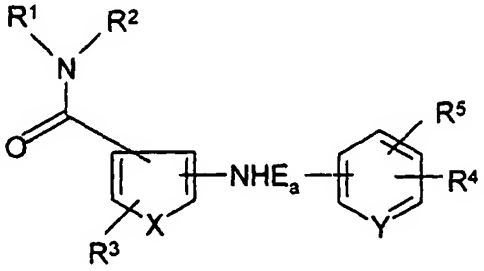
(II)

or its salt with a compound of the formula:



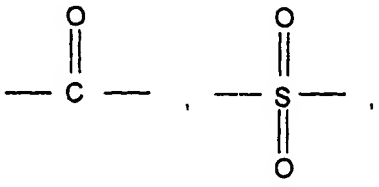
(III)

or its reactive derivative at the carboxy group or the sulfo group, or a salt thereof to provide a compound of the formula:



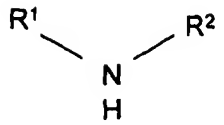
(Ia)

or its salt, in the above formulas,
R^1, R^2, R^3, R^4, R^5, X and Y are each as defined above, and
Ea is



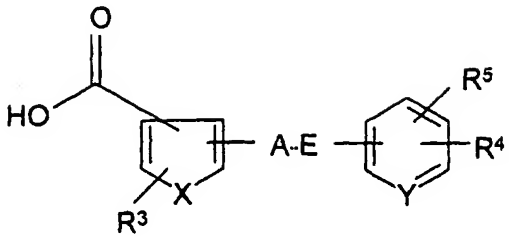
or

2) reacting a compound of the formula:



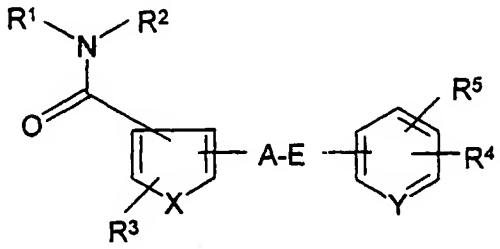
(IV)

or its salt with a compound of the formula :



(V)

or its reactive derivative at the carboxy group or a salt thereof to provide a compound of the formula:



(I)

or its salt, in the above formulas,
R^1, R^2, R^3, R^4, R^5, A, E, X and Y are each as defined above.

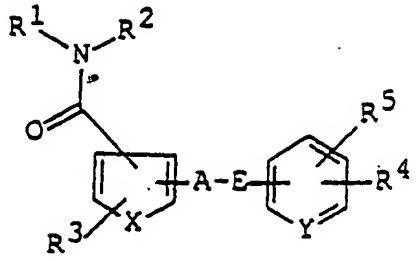
6. A pharmaceutical composition comprising a compound of claim 1, as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.

7. A compound of claim 1 for use as a medicament.

8. Use of a compound of claim 1 for the manufacture of a medicament for treating and/or preventing hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, cerebrovascular disease, Meniere's syndrome or motion sickness in human beings or animals.

Patentansprüche

1. Verbindung der Formel



(I)

wobei

R^1 Aryl, Cyclo (C_3 - C_6) alkyl, Pyridyl oder Thienyl ist,
wobei jede Gruppe mit einem oder mehreren Substituenten substituiert sein kann, die aus der Gruppe ausgewählt sind, die besteht aus Halogen; Hydroxy; Nitro; Amino; Acyl; substituiertem Acyl; Acyl (C_1 - C_6) alkylsulfinyl; Acyl (C_1 - C_6) alkylsulfonyl; Acyloxy; C_1 - C_6 Alkylamino (C_1 - C_6) alkylcarbamoyloxy; Aryl; Cyano; einer heterocyklischen Gruppe;
C_2 - C_6 Alkenyl, optional substituiert mit Acyl, substituiertem Acyl, Aryl oder Acyl-substituiertem Aryl;
C_2 - C_6 Alkinyl, optional substituiert mit Amino, Acylamino oder substituiertem Acylamino;
C_1 - C_6 Alkyl, optional substituiert mit Halogen, Amino, C_1 - C_6Alkylamino, Acylamino, substituiertem Acylamino, Hydroxy, Acyloxy, Acyl (C_1 - C_6) alkanoyloxy, Acyl, substituiertem Acyl, Acyl (C_1 - C_6) alkoxyimino, Aryl oder Acyl-substituiertem Aryl;
C_1 - C_6 Alkylthio, optional substituiert mit Acyl oder substituiertem Acyl;
Alkoxy, optional substituiert mit Aryl, substituiertem Aryl, Hydroxy, Acyloxy, Amino, C_1 - C_6 Alkylamino, geschütztem Amino, einer heterozyklischen Gruppe, Acyl-substituiertem Pyridyl, substituiertem Acyl-substituiertem Pyridyl, Halogen, Acyl (C_1 - C_6) alkylamino, N-geschütztem Acyl (C_1 - C_6) alkylamino, N-Acyl (C_1 - C_6) alkyl-N- C_1-C_6 alkylamino, Acyl, substituiertem Acyl, Acylamino, substituiertem Acylamino, C_1 - C_6 Alkylhydrazinocarbonylamino, Hydroxyimino, Acyl (C_1 - C_6) alkoxyimino, substituiertem Acyl(C_1-C_6) alkoxyimino, Acyl (C_1-C_6) alkoxy, Guanidino oder N-geschütztem Guanidino; und
C_2 - C_6 Alkenyloxy, optional substituiert mit Acyl oder substituiertem Acyl;

R^2 Wasserstoff; C_1 - C_6 Alkyl, optional substituiert mit Hydroxy, Aryl oder Acyl;oder Cyclo (C_3 - C_6) alkyl ist;

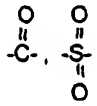
R^3 Wasserstoff; Halogen; Hydroxy; Acyloxy; substituiertes Acyloxy; C_1 - C_6 Alkyl, optional substituiert mit Hydroxy oder C_1 - C_6 Alkoxy; C_1 - C_6 Alkoxy, optional substituiert mit Aryl, Amino, geschütztem Amino, Acyl, Hydroxy, Cyano, oder C_1 - C_6 Alkylthio; Nitro; Amino; Acyl; substituiertes Acyl; oder Cyclo (C_1 - C_6) alkyloxy ist;

R^4 Wasserstoff; Halogen; Nitro; Amino; geschütztes Amino; C_1 - C_6 Alkylamino; Acyloxy; Amino (C_1 - C_6) alkylamino; N-geschütztes Amino (C_1 - C_6) alkylamino; C_1 - C_6 Alkoxy, optional substituiert mit Hydroxy, Aryl, substituiertem Aryl, Acyl, substituiertem Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, einer heterozyklischen Gruppe oder Guanidino;
C_1 - C_6 Alkylthio, optional substituiert mit Acyl, substituiertem Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, einer heterozyklischen Gruppe, Hydroxy, C_1 - C_6 Alkylsulfonyloxy, Arylsulfonyloxy, Ar (C_1 - C_6) alkoxy oder substituiertem Ar (C_1 - C_6) alkoxy; C_1 - C_6 Alkyl, substituiert mit Acyl, substituiertem Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, eine heterozyklische Gruppe, Hydroxy, C_1 - C_6 Alkylsulfonyloxy oder Arylsulfonyloxy; C_2 - C_6 Alkenyl, optional substituiert mit Acyl; C_2 - C_6 Alkinyl, optional substituiert mit Hydroxy, Amino, geschütztem Amino, C_1 - C_6 Alkylsulfonyloxy oder Arylsulfonyloxy; Amino (C_1 - C_6) alkylsulfonyl; N-geschütztes Amino (C_1 - C_6) alkylsulfonyl; C_1 - C_6 Alkylaminosulfonyl; ein heterocyclisches Sulfonyl; Amino (C_1 - C_6) alkylsulfinyl; N-geschütztes Amino (C_1 - C_6) alkylsulfinyl; Piperidyloxy; oder N-geschütztes Piperidyloxy ist;

R^5 Wasserstoff, C_1 - C_6 Alkyl, C_1 - C_6 Alkoxy oder Halogen ist;

A eine einfache Bindung, O oder NH ist;

E C_1 - C_6 Alkylen, C_2 - C_6 Alkenylen,



oder eine Gruppe der Formel -G-J- ist, wobei
G C_1 - C_6 Alkylen und J O oder

ist (worin R^6 Wasserstoff oder eine N-Schutzgruppe ist);
X -CH=CH-, -CH=N- oder S ist; und
Y CH oder N ist;

und pharmazeutisch akzeptable Salze davon.

2. Verbindung nach Anspruch 1, wobei

R^1 Aryl ist, das mit C_1 - C_6 Alkoxy substituiert sein kann, welches optional mit Acylamino oder Acyl substituiert ist;
R^2 C_1 - C_6 Alkyl ist;
R^3 Wasserstoff, C_1 - C_6 Alkyl oder C_1 - C_6 Alkoxy ist;
R^4 Wasserstoff oder C_1 - C_6 Alkoxy oder C_1 - C_6 Alkylthio ist, wobei jedes mit Hydroxy, Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, geschütztem Amino oder einer heterozyklischen Gruppe substituiert sein kann;
R^5 Wasserstoff, C_1 - C_6 Alkyl, C_1 - C_6 Alkoxy oder Halogen ist;
A NH ist;
E

ist;
X -CH=CH- ist; und
Y CH ist.

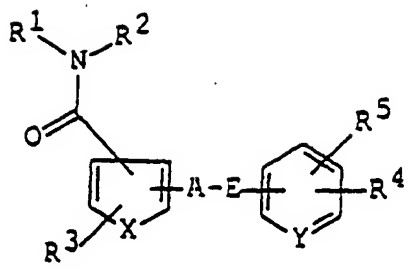
3. Verbindung nach Anspruch 2, wobei

R^1 Phenyl oder Tolyl ist, wobei jedes mit C_1 - C_6 Alkoxy substituiert ist, das mit Acyl substituiert ist;
R^3 C_1 - C_6 Alkyl oder C_1 - C_6 Alkoxy ist;
R^4 C_1 - C_6 Alkoxy oder C_1 - C_6 Alkylthio ist, wobei jedes mit Amino oder Hydroxy substituiert ist.

4. Verbindung nach Anspruch 3, wobei

R^1 Phenyl oder Tolyl ist, wobei jedes mit C_1 - C_6 Alkoxy substituiert ist, das mit N-(C_1 - C_6) alkylpiperazinylcarbonyl substituiert ist;
R^3 C_1 - C_6 Alkoxy ist;
R^4 C_1 - C_6 Alkoxy ist, das mit Amino substituiert ist; und
R^5 Wasserstoff ist.

5. Verfahren zur Herstellung der Formel:



(I)

wobei

R^1 Aryl, Cyclo (C_3 - C_6) alkyl, Pyridyl oder Thienyl ist,
wobei jede Gruppe mit einem oder mehreren Substituenten substituiert sein kann, die aus der Gruppe ausgewählt sind, die besteht aus Halogen; Hydroxy; Nitro; Amino; Acyl; substituiertem Acyl; Acyl (C_1 - C_6) alkylsulfinyl; Acyl (C_1 - C_6) alkylsulfonyl; Acyloxy; C_1 - C_6 Alkylamino (C_1 - C_6) alkylcarbamoyloxy; Aryl; Cyano; einer heterocyklischen Gruppe;
C_2 - C_6 Alkenyl, optional substituiert mit Acyl, substituiertem Acyl, Aryl oder Acyl-substituiertem Aryl;
C_2 - C_6 Alkinyl, optional substituiert mit Amino, Acylamino oder substituiertem Acylamino;
C_1 - C_6 Alkyl, optional substituiert mit Halogen, Amino, C_1 -C_6 Alkylamino, Acylamino, substituiertem Acylamino, Hydroxy, Acyloxy, Acyl (C_1 - C_6) alkanoyloxy, Acyl, substituiertem Acyl, Acyl (C_1 - C_6) alkoxyimino, Aryl oder Acyl-substitueirtem Aryl;
C_1 - C_6 Alkylthio, optional substituiert mit Acyl oder substituiertem Acyl;
Alkoxy, optional substituiert mit Aryl, substituiertem Aryl, Hydroxy, Acyloxy, Amino, C_1 - C_6 Alkylamino, geschütztem Amino, einer heterozyklischen Gruppe, Acyl-substituiertem Pyridyl, substituiertem Acyl-substituiertem Pyridyl, Halogen, Acyl (C_1 - C_6) alkylamino, N-geschütztem Acyl (C_1 - C_6) alkylamino, N-Acyl (C_1 - C_6) alkyl-N- C_1-C_6 alkylamino, Acyl, substituiertem Acyl, Acylamino, substituiertem Acylamino, C_1 - C_6 Alkylhydrazinocarbonylamino, Hydroxyimino, Acyl (C_1 - C_6) alkoxyimino, substituiertem Acyl (C_1 - C_6) alkoxyimino, Acyl (C_1 - C_6) alkoxy, Guanidino oder N-geschütztem Guanidino; und
C_2 - C_6 Alkenyloxy, optional substituiert mit Acyl oder substituertem Acyl;

R^2 Wasserstoff; C_1 - C_6 Alkyl, optional substituiert mit Hydroxy, Aryl oder Acyl; oder Cyclo (C_3 - C_6) alkyl ist;

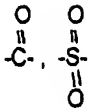
R^3 Wasserstoff; Halogen; Hydroxy; Acyloxy; substituiertem Acyloxy; C_1 - C_6 Alkyl, optional substituiert mit Hydroxy oder C_1 - C_6 Alkoxy; C_1 - C_6 Alkoxy, optional substituiert mit Aryl, Amino, geschütztem Amino, Acyl, Hydroxy, Cyano, oder C_1 - C_6 Alkylthio; Nitro; Amino; Acyl; substituiertem Acyl; oder Cyclo (C_1 - C_6) alkyloxy ist;

R^4 Wasserstoff; Halogen; Nitro; Amino; geschütztes Amino; C_1 - C_6 Alkylamino; Acyloxy; Amino (C_1 - C_6) alkylamino; N-geschütztes Amino (C_1 - C_6) alkylamino; C_1 - C_6 Alkoxy, optional substituiert mit Hydroxy, Aryl, substituiertem Aryl, Acyl, substituiertem Acyl Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, einer heterozyklischen Gruppe oder Guanidino; C_1 - C_6 Alkylthio, optional substituiert mit Acyl, substituiertem Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, einer heterozyklischen Gruppe, Hydroxy, C_1 - C_6 Alkylsulfonyloxy, Arylsulfonyloxy, Ar (C_1 - C_6) alkoxy oder substituiertem Ar (C_1 - C_6) alkoxy; C_1 - C_6 Alkyl, substituiert mit Acyl, substituiertem Acyl, Amino, C_1 - C_6 Alkylamino, Acylamino, substituiertem Acylamino, geschütztem Amino, einer heterozyklischen Gruppe, Hydroxy, C_1 - C_6 Alkylsulfonyloxy oder Arylsulfonyloxy; C_2 - C_6 Alkenyl, optional substituiert mit Acyl; C_2 - C_6 Alkinyl, optional substituiert mit Hydroxy, Amino, geschütztem Amino, C_1 - C_6 Alkylsulfonyloxy oder Arylsulfonyloxy; Amino (C_1 - C_6) alkylsulfonyl; N-geschütztes Amino (C_1 - C_6) alkylsulfonyl; C_1 - C_6 Alkylaminosulfonyl; ein heterocyclisches Sulfonyl; Amino (C_1 - C_6) alkylsulfinyl; N-geschütztes Amino (C_1 - C_6) alkylsulfinyl; Piperidyloxy; oder N-geschütztes Piperidyloxy ist;

R^5 Wasserstoff, C_1 - C_6 Alkyl, C_1 - C_6 Alkoxy oder Halogen ist;

A eine einfache Bindung, O oder NH ist;

E C_1 - C_6 Alkylen, C_2 - C_6 Alkenylen,

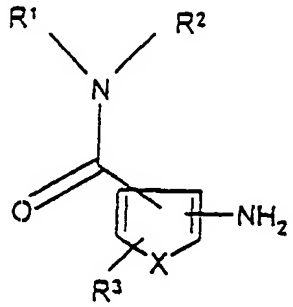


oder eine Gruppe der Formel
-G-J- ist, wobei
G C_1 - C_6 Alkylen und J O oder

ist (worin R^6 ein Wasserstoff oder eine N-Schutzgruppe ist);
X -CH=CH-, -CH=N- oder S ist und
Y CH oder N ist;

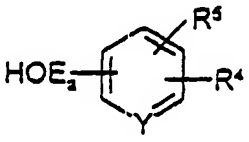
oder von pharmazeutisch akzeptablen Salzen davon,
wobei das Verfahren umfasst

1) Reagieren einer Verbindung der Formel:



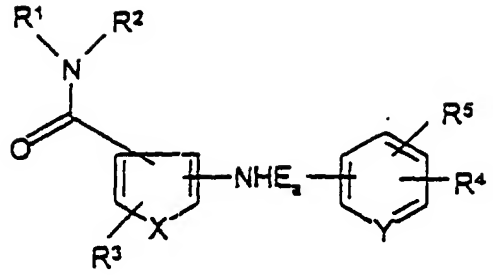
(II)

oder ihres Salzes mit einer Verbindung der Formel:



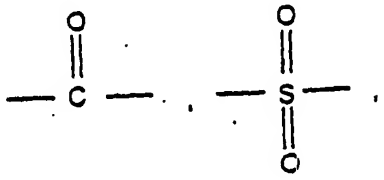
(III)

oder ihres reaktiven Derivats an der Carboxygruppe oder der Sulfogruppe, oder eines Salzes davon, um eine Verbindung der Formel:



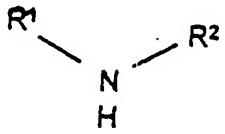
(Ia)

oder ihres Salzes bereitzustellen, wobei in den obigen Formeln R^1, R^2, R^3, R^4, R^5, X und Y jeweils wie oben definiert sind, und Ea



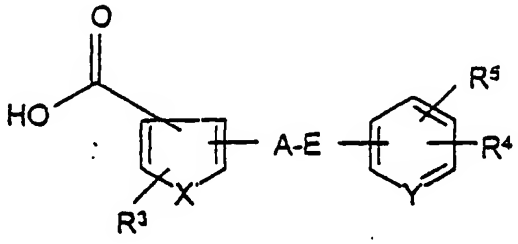
ist, oder

2) Reagieren einer Verbindung der Formel:



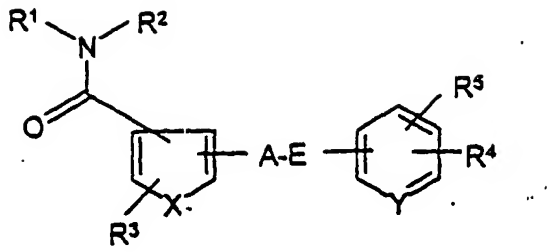
(IV)

oder ihres Salzes mit einer Verbindung der Formel:



(V)

oder ihres reaktiven Derivats an der Carboxygruppe oder eines Salzes davon, um eine Verbindung der Formel:



(I)

oder ihres Salzes bereitzustellen, wobei in den obigen Formeln
R^1, R^2, R^3, R^4, R^5, A, E, X und Y jeweils wie oben definiert sind.

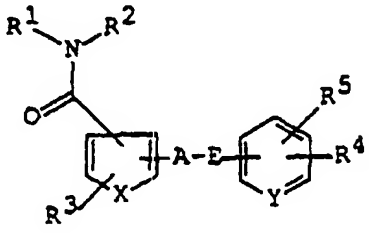
6. Pharmazeutische Zusammensetzung, umfassend eine Verbindung nach Anspruch 1 als einen Wirkstoff in Assoziation mit einem pharmazeutisch akzeptablen, im wesentlichen nicht-toxischen Träger oder Trägerstoff.

7. Verbindung nach Anspruch 1 für die Verwendung als Medikament.

8. Verwendung einer Verbindung nach Anspruch 1 für die Herstellung eines Medikamentes für die Behandlung und/oder Verhinderung von Hypertonie, Herzversagen, Niereninsuffizienz, Ödem, Aszites, Vasopressin-Parasekretionssyndrom, Leberzirrhose, Hyponatriämie, Hypokaliämie, diabetischen Kreislaufstörungen, Stoffwechselstörung, cerebrovaskulärer Krankheit, Morbus Meniere oder Reisekrankheit beim Menschen oder Tier.

Revendications

1. Composé de formule :



(I)

dans laquelle

R^1 est un aryle, un cycloalkyle (en C_3-C_6), un pyridyle ou un thiényle,
dont chacun peut être substitué par un ou des substituants choisis parmi le groupe constitué d'un halogène, d'un hydroxyde, d'un nitro, d'un amino, d'un acyle, d'un acyle substitué,
un acylalkyl (en C1-C6) sulfinyle, un acylalkyl (en C1-C6) sulfonyle, un acyloxy, un alkyl (en C1-C6) aminoalkyl (en C1-C6) carbamoyloxy, un aryle, un cyano, un groupement hétérocyclique,
un alcényle (en C2-C6) substitué facultativement par un acyle, un acyle substitué, un aryle ou un aryle substitué par un acyle,
un alcynyle (en C2-C6) substitué facultativement par un amino, un acylamino ou un acylamino substitué,
un alkyle (en C1-C6) substitué facultativement par un halogène, un amino, un alkyl (en C1-C6) amino, un acylamino, un acylamino substitué, un hydroxy, un acyloxy, un acylalcanoyl (en C1-C6) oxy, un acyle, un acyle substitué, un acylalcoxy (en C1-C6) imino, un aryle ou un aryle substitué par un acyle,
un alkyl (en C1-C6) thio substitué facultativement par un acyle ou un acyle substitué,
un alcoxy substitué facultativement par un aryle, un aryle substitué, un hydroxy, un acyloxy, un amino, un alkyl (en C1-C6) amino, un amino protégé , un groupement hétérocyclique, un pyridyle substitué par un acyle,

un pyridyle substitué par un acyle substitué, un halogène, un acylalkyl (en C1-C6) amino, un acylalkyl (en C1-C6) amino à N protégé, un N -acylakyl (en C1-C6) -N -alkyl (en C1-C6) amino, un acyle, un acyle substitué, un acylamino, un acylamino substitué, un alkyl (en C1-C6) hydrazinocarbonylamino, un hydroxy -imino, un acylalcoxy (en C1-C6) imino, un acylalcoxy (en C1-C6) imino substitué, un acylalcoxy (en C1-C6), un guanidino ou un guanidino à N protégé, et
un alcényl (en C2-C6) oxy substitué facultativement par un acyle ou un acyle substitué,

R^2 est un hydrogène, un alkyle (en C_1-C_6) substitué facultativement par un hydroxy, un aryle ou un acyle, ou un cycloalkyle (en C_3-C_6),

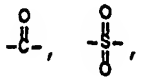
R^3 est un hydrogène, un halogène, un hydroxy, un acyloxy, un acyloxy substitué, un alkyle (en C_1-C_6) substitué facultativement par un hydroxy ou un alcoxy (en C_1-C_6), un alcoxy (en C_1-C_6) substitué facultativement par un aryle, un amino, un amino protégé, un acyle, un hydroxy, un cyano, ou un alkyl (en C_1-C_6) thio, un nitro, un amino, un acyle, un acyle substitué, ou un cycloalkyl (en C_3-C_6) oxy,

R^4 est un hydroxy, un halogène, un nitro, un amino, un amino protégé, un alkyl (en C_1-C_6) amino, un acyloxy, un aminoalkyl (en C_1-C_6) amino, un aminoalkyl (en C_1-C_6) amino à N protégé, un alcoxy (en C_1-C_6) substitué facultativement par un hydroxy, un aryle, un aryle substitué, un acyle, un acyle substitué, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique ou un guanidino, un alkyl (en C_1-C_6) thio substitué facultativement par un acyle, un acyle substitué, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique, un hydroxy, un alkyl (en C_1-C_6) sulfonyloxy, un arylsulfonyloxy, un aralcoxy (en C_1-C_6) ou un aralcoxy (en C_1-C_6) substitué, un alkyle (en C_1-C_6) substitué par un acyle, un acyle substitué, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique, un hydroxy, un alkyl (en C_1-C_6) sulfonyloxy ou un arylsulfonyloxy, un alcényle (en C_2-C_6) substitué facultativement par un acyle, un alcynyle (en C_2-C_6) substitué facultativement par un hydroxy, un amino, un amino protégé, un alkyl (en C_1-C_6) sulfonyloxy ou un arylsulfonyloxy, un aminoalkyl (en C_1-C_6) sulfonyle, un aminoalkyl (en C_1-C_6) sulfonyle à N protégé, un alkyl (en C_1-C_6) aminosulfonyle, un sulfonyle hétérocyclique, un aminoalkyl (en C_1-C_6) sulfinyle, un aminoalkyl (en C_1-C_6) sulfinyle à N protégé, un pipéridyloxy, ou un pipéridyloxy à N protégé,

R^5 est un hydrogène, un alkyle (en C_1-C_6), un alcoxy (en C_1-C_6) ou un halogène,

A est une simple liaison, O ou NH,

E est un alcylène (en C_1-C_6), un alcénylène (en C_2-C_6),



ou un groupement de formule :

-G-J-

dans laquelle G est un alcylène (en C_1-C_6) et J est O ou

(dans laquelle R^6 est un hydrogène ou un groupement protecteur de N),

X est -CH=CH-, -CH=N- ou S, et

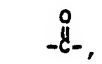
Y est CH ou N,

et sels pharmaceutiquement acceptables de celui-ci.

2. Composé selon la revendication 1, dans lequel

R^1 est un aryle qui peut être substitué par un alcoxy (en C_1-C_6) substitué facultativement par un acylamino ou

un acyle,
R^2 est un alkyle (en C_1-C_6),
R^3 est un hydrogène, un alkyle (en C_1-C_6) ou un alcoxy (en C_1-C_6),
R^4 est un hydroxy, ou un alcoxy (en C_1-C_6) ou un alkyl (en C_1-C_6) thio, dont chacun peut être substitué par un hydroxy, un acyle, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un amino protégé ou un groupement hétérocyclique,
R^5 est un hydrogène, un alkyle (en C_1-C_6), un alcoxy (en C_1-C_6) ou un halogène,
A est NH,
E est



X est -CH=CH-, et
Y est CH.

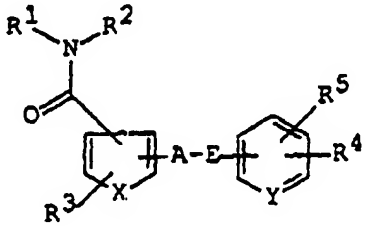
3. Composé selon la revendication 2, dans lequel

R^1 est un phényle ou un tolyle, dont chacun est substitué par un alcoxy (en C_1-C_6) substitué par un acyle,
R^3 est un alkyle (en C_1-C_6) ou un alcoxy (en C_1-C_6),
R^4 est un alcoxy (en C_1-C_6) ou un alkyl (en C_1-C_6) thio, dont chacun est substitué par un amino ou un hydroxy.

4. Composé selon la revendication 3, dans lequel

R^1 est un phényle ou un tollyle, dont chacun est substitué par un alcoxy (en C_1-C_6) substitué par un N-alkyl (en C_1-C_6) pipérazinylcarbonyle,
R^3 est un alcoxy (en C_1-C_6),
R^4 est un alcoxy (en C_1-C_6) substitué par un amino, et
R^5 est un hydrogène.

5. Procédé destiné à la préparation de la formule :



(I)

dans laquelle

R^1 est un aryle, un cycloalkyle (en C_3-C_6), un pyridyle ou un thiényle,
dont chacun peut être substitué par un ou des substituants choisis parmi le groupe constitué d'un halogène, d'un hydroxy, d'un nitro, d'un amino, d'un acyle, d'un acyle substitué,
un acylalkyl (en C_1-C_6) sulfinyle, un acylalkyl (en C_1-C_6) sulfonyle, un acyloxy, un alkyl (en C_1-C_6) aminoalkyl (en C_1-C_6) carbamoyloxy, un aryle, un cyano, un groupement hétérocyclique, un alcényle (en C_2-C_6) substitué facultativement par un acyle, un acyle substitué, un aryle ou un aryle substitué par un acyle,
un alcynyle (en C_2-C_6) substitué facultativement par un amino, un acylamino ou un acylamino substitué, un alkyle (en C_1-C_6) substitué facultativement par un halogène, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un hydroxy, un acyloxy, un acylalcanoyl (en C_1-C_6) oxy, un acyle, un acyle substitué, un acylalcoxy (en C_1-C_6) imino, un aryle ou un aryle substitué par un acyle,

un alkyl (en C_1-C_6) thio substitué facultativement par un acyle ou un acyle substitué, un alcoxy substitué facultativement par un aryle, un aryle substitué, un hydroxy, un acyloxy, un amino, un alkyl (en C_1-C_6) amino, un amino protégé, un groupement hétérocyclique, un pyridyle substitué par un acyle, un pyridyle substitué par un acyle substitué, un halogène, un acylalkyl (en C_1-C_6) amino, un acylalkyl (en C_1-C_6) amino à N protégé, un N-acylalkyl (en C_1-C_6) -N-alkyl (en C_1-C_6) amino, un acyle, un acyle substitué, un acylamino, un acylamino substitué, un alkyl (en C_1-C_6) hydrazinocarbonylamino, un hydroxy-imino, un acylalcoxy (en C_1-C_6) imino, un acylalcoxy (en C_1-C_6) imino substitué, un acylalcoxy (en C_1-C_6), un guanidino ou un guanidino à N protégé, et

un alcényloxy (en C_2-C_6) substitué facultativement par un acyle ou un acyle substitué,

R^2 est un hydrogène, un alkyle (en C_1-C_6) substitué facultativement par un hydroxy, un aryle ou un acyle, ou un cycloalkyle (en C_3-C_6),

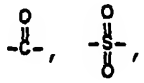
R^3 est un hydrogène, un halogène, un hydroxy, un acyloxy, un acyloxy substitué, un alkyle (en C_1-C_6) substitué facultativement par un hydroxy ou un alcoxy (en C_1-C_6), un alcoxy (en C_1-C_6) substitué facultativement par un aryle, un amino, un amino protégé, un acyle, un hydroxy, un cyano, ou un alkyl (en C_1-C_6) thio, un nitro, un amino, un acyle, un acyle substitué, ou un cycloalkyl (en C_3-C_6) oxy,

R^4 est un hydroxy, un halogène, un nitro, un amino, un amino protégé, un alkyl (en C_1-C_6) amino, un acyloxy, un aminoalkyl (en C_1-C_6) amino, un aminoalkyl (en C_1-C_6) amino à N protégé, un alcoxy (en C_1-C_6) substitué facultativement par un hydroxy, un aryle, un aryle substitué, un acyle, un acyle substitué, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique ou un guanidino, un alkyl (en C_1-C_6) thio substitué facultativement par un acyle, un acyle substitué, un aminoalkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique, un hydroxy, un alkyl (en C_1-C_6) sulfonyloxy, un arylsulfonyloxy, un aralcoxy (en C_1-C_6) ou un aralcoxy (en C_1-C_6) substitué, un alkyle (en C_1-C_6) substitué par un acyle, un acyle substitué, un amino, un alkyl (en C_1-C_6) amino, un acylamino, un acylamino substitué, un amino protégé, un groupement hétérocyclique, un hydroxy, un alkyl (en C_1-C_6) sulfonyloxy ou un arylsulfonyloxy, un alcényle (en C_2-C_6) substitué facultativement par un acyle, un alcynyle (en C_2-C_6) substitué facultativement par un hydroxy, un amino, un amino protégé, un alkyl (en C_1-C_6) sulfonyloxy ou un arylsulfonyloxy, un aminoalkyl (en C_1-C_6) sulfonyle, un aminoalkyl (en C_1-C_6) sulfonyle à N protégé, un alkyl (en C_1-C_6) aminosulfonyle, un sulfonyle hétérocyclique, un aminoalkyl (en C_1-C_6) sulfinyle, un aminoalkyl (en C_1-C_6) sulfinyle à N protégé, un pipéridyloxy, ou un pipéridyloxy à N protégé,

R^5 est un hydrogène, un alkyle (en C_1-C_6), un alcoxy (en C_1-C_6) ou un halogène,

A est une simple liaison, O ou NH,

E est un alcylène (en C_1-C_6), un alcénylène (en C_2-C_6),



ou un groupement de formule :

-G-J-

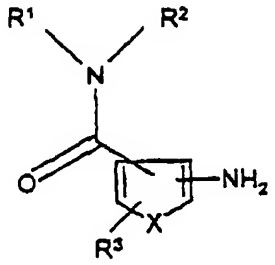
dans laquelle G est un alcylène (en C_1-C_6) et J est O ou

(dans laquelle R^6 est un hydrogène ou un groupement protecteur de N),

X est -CH=CH-, -CH=N- ou S, et
Y est CH ou N,

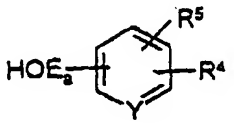
et des sels pharmaceutiquement acceptables de celle-ci,
qui comprend,

1) la réaction d'un composé de formule :



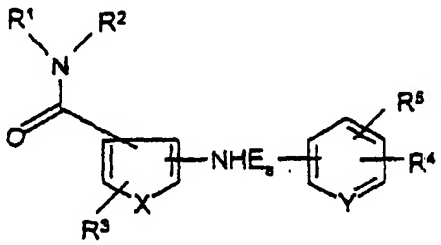
(II)

ou de son sel avec un composé de formule :



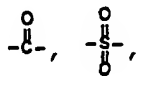
(III)

ou son dérivé réactif au niveau du groupement carboxy ou du groupement sulfo, ou un sel de celui-ci pour donner un composé de formule :



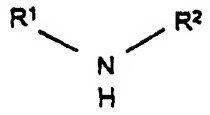
(Ia)

ou son sel, dans les formules ci-dessus,
R^1, R^2, R^3, R^4, R^5, X et Y sont chacun tels que définis ci-dessus, et
Ea est



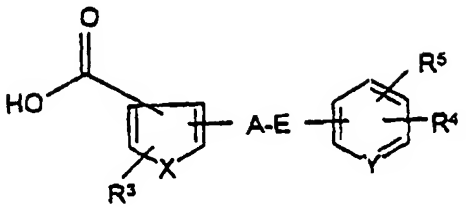
ou

2) la réaction d'un composé de formule :



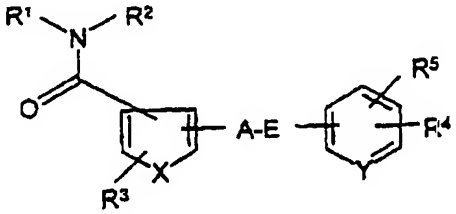
(IV)

ou de son sel avec un composé de formule :



(V)

ou son dérivé réactif au niveau du groupement carboxy ou un sel de celui-ci pour donner un composé de formule :



(I)

ou son sel, dans les formules ci-dessus,
R^1, R^2, R^3, R^4, R^5, A, E, X et Y sont chacun tels que définis ci-dessus.

6. Composition pharmaceutique comprenant un composé selon la revendication 1, en tant que principe actif, en association avec un support ou un excipient pharmaceutiquement acceptables, substantiellement non toxiques.

7. Composé selon la revendication 1, destiné à une utilisation en tant que médicament.

8. Utilisation d'un composé selon la revendication 1, pour la fabrication d'un médicament destiné au traitement et/ou à la prévention de l'hypertension, d'une insuffisance cardiaque, une insuffisance rénale, un oedème, une ascite, le syndrome de la parasécrétion de la vasopressine, une cirrhose du foie, une hyponatrémie, une hypokaliémie, un diabète, un trouble de la circulation, une maladie cérébro-vasculaire, un syndrome de Ménière ou le mal des transports chez les êtres humains ou chez les animaux.